A PROSPECTIVE OPEN LABELLED PHASE-II NON RANDOMIZED CLINICAL STUDY OF "NELLI KUDINEER" FOR

"RATHAMOOLAM"

(BLEEDING HEMORRHOIDS)

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GOVERNMENT SIDDHA MEDICAL COLLEGE

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"A PROSPECTIVE OPEN LABELLED PHASE-II NON RANDOMIZED CLINICAL STUDY OF NELLI KUDINEER FOR RATHAMOOLAM (BLEEDING HEMORRHOIDS)"** is a bonafide work done by **DR.SUMAYYA.M (Reg. No.321611010),** Govt. Siddha Medical College, Palayamkottai, in partial fulfilment of the university rules and regulations for the award of **M.D (S), POTHU MARUTHUVAM (BRANCH-I**) under my guidance and supervision during the academic year **OCTOBER 2016-2019.**

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CERTIFICATE I

Certified that I have gone through the dissertation entitled **"A PROSPECTIVE OPEN LABELLED PHASE-II NON RANDOMIZED CLINICAL STUDY OF NELLI KUDINEER FOR RATHAMOOLAM (BLEEDING HEMORRHOIDS)"** submitted by **Dr.SUMAYYA.M (Reg. No.321611010), student of final year M.D(S), Department of Pothu Maruthuvam (Branch-I)** of this college and the dissertation work has been carried out by the individual only. This dissertation did not submit and approve earlier.

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CERTIFICATE II

This is to certify that this dissertation entitled **"A PROSPECTIVE OPEN LABELLED PHASE-II NON RANDOMIZED CLINICAL STUDY OF NELLI KUDINEER FOR RATHAMOOLAM (BLEEDING HEMORRHOIDS)"** submitted by **Dr.SUMAYYA.M (Reg. No.321611010),** for the award of M.D.(S), Pothumaruthuvam Department (Branch I). I personally verified the urkund.com website for the purpose of Plagiarism check. I found that the uploaded thesis contains from Introduction to Conclusion pages and result shows **2%** of **Plagiarism** in the dissertation.

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DECLARATION BY THE CANDIDATE

I, **Dr. SUMAYYA.M.** declared that the thesis entitled **"A PROSPECTIVE OPEN LABELLED PHASE-II NON RANDOMIZED CLINICAL STUDY OF NELLI KUDINEER FOR RATHAMOOLAM (BLEEDING HEMORRHOIDS)"** submitted by me for the award of Degree of Doctor of Medicine (Siddha) from Government Siddha Medical College, Palayamkottai, Tirunelveli, Tamil Nadu (The Tamil Nadu Dr. M.G.R. Medical University, Chennai). The record of research work carried out by me under the supervision and guidance of **Prof.Dr.A.Manoharan, M.D (S), (Ph.D),** Head of Department of PothuMaruthuvam, Govt. Siddha Medical College, Palayamkottai. This work has not formed the basis for the award of any other degree, diploma, associate ship, fellowship or any other similar titles in this university or any other university or institution of higher learning.

Place : Palayamkottai Signature of the candidate

Date : **(Dr.SUMAYYA.M)**

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ABBREVIATIONS

ABTS	-	2,2-Azino-Bis-3-Ethyl-benzothiazoline-6-sulfonic acid
ALT	-	Alanine Transaminase
AST	-	Aspartate Amino Transferase
ATP	-	Alkaline Phosphate
CRP	-	C-reactive protein
CTRI	-	Clinical Trial Registry of India
DMBA	-	di-methyl benza anthracene
EO	-	Emblica officinalis
GIT	-	Gastro intestinal tract
HDL	-	High Density Lipids
HPTLC	-	High performance liquid chromatography
IAEC	-	Institutional Animal Ethical Committee
IEC	-	Institutional Ethical Committee
KC	-	Kudineer Chooranam
LD	-	Lethal Dose
NK	-	Nelli Kudineer
OECD	-	Organisation for Economic Co-operation and Development
PAA	-	Percentage Analysis Activity
PEE	-	Phyllanthus Emblica extract
PK	-	Pitha Kapam
RM	-	Rathamoolam
SEM	-	Standard Error of Mean
SH	-	Stapled Hemorrhoidopexy
STD	-	Sexually transmitted disease
TA	-	Tannic Acid
TC	-	Total count
TG	-	Triglycerides
UroA	-	Urolithin A
VP	-	Vatha Pitham
YVC	-	Yugi Vaidhya Chinthamani
ZIC	-	Zone of Inhibition

ABSTRACT

The first known mention of the disease Rathamoolam (bleeding Hemorrhoids) is from 1700 BC Egyptian papyrus. The nature, etiology, types, clinical features and prognosis of Rathamoolam has mentioned in Yugimuni's literature. The prevalence of Hemorrhoids ranges from 4.4% in the general population to 36.4% in general practice. Prevalence of Hemorrhoids in India according to recent survey is about 40 million. It is now considered a major cause of morbidity and imposes burden on the society both economically and socially. Males and Females are affected with about equal frequency.

Siddha recommended the Compatible diet and activities, cost effective easily available preparations and management of **Rathamoolam** (RM). **Nelli Kudineer** (NK) is one of the effective Siddha herbal preparations, mentioned in Gunapadam Moolikai. 40 patients including OP & IP, both genders were selected according to the criteria mentioned in the proforma and they were administered with trial drug Nelli Kudineer 100ml in the morning before food for one month.

The pre clinical and clinical evaluations of Nelli Kudineer were carried out and results were showed its effectiveness for Rathamoolam. The panchabootham and its relations with gunam of Nelli Kudineer were proven for their activity in relieving the symptoms of Rathamoolam.

The gradation of result was found to be **good** improvement in **73%** cases, **moderate** improvement in **23%** cases and **mild** improvement in **4%** cases.

CHAPTER-1
INTRODUCTION

Through the Spiritual, Intellectual and Systematic work of Siddhars, Siddha system developed. Everything in the universe is Iymboothamayam (Panchaboothas-five elements).The Divine power guards the soul, mind and body. The body is constituted by the Panchabootha combinations and permutation is the supports for the soul are the 3 thathus namely Vatham, Pitham and Kapam. It attains 3 Gunas through Vaayu, Theyu and Appu. Ninety six thathuvas attained through an Embryo. It protects and supports the body and soul according to the ancient texts.

Any vitiation from normal condition of Uyirthathu which deranges Udalthathu, any of 96 Thathuvams partially or totally and is manifested by characteristic symptoms and signs is called Noi (Diseases).Even though there are only 3 dhosas, the diseases produced are many and can be grouped generally as Vali, Azhal, Iyam and Thontham. But Yugimuni revised this approach and classified disease based either on three humours (Kutram), Etiology, Clinical signs and symptoms for convenience and easy understanding of the disease. The widely accepted number of diseases according to Agasthiyar Ratna Churukka Naadi nool is about 4448.

My selected topic is Rathamoolam (Bleeding Hemorrhoids) for the dissertation work. It comes under the heading of Eruvaaimulai noi/Moola noi (Anorectal diseases).Yugimuni classified Moolam into 21 types and Theran classified Moolam into 10 types. This topic Rathamoolam comes under Yugimuni classification. He described the clinical features of Rathamoolam are Pain in and around the Umbilicus and spurting of blood from rectum and anal canal which looks like splash in the pan, Weight loss, Anaemia, Easy fatigability, Oedema, Throbbing chest pain, Headache ,Drowsiness and Yellowish eye. Rathamoolam symptoms can be correlated in Modern medicine is Bleeding Hemorrhoids.

Hemorrhoids (Greek:haima-blood,rhoo-flowing) are known as Moolam in Siddha and commonly known as Piles (Latin:pila-ball). Hemorrhoid is the saccular dilatation of Internal rectal venous plexus or Hemorrhoidal plexus, abnormal distension of Arterio-venous anastomosis, Prolapse of the cushions and surrounding connective tissue. Various factors responsible for the Hemorrhoids are Poor support to

veins, absence of valves in veins, compression of veins and direct transmission of the increased portal pressure at the Porto systemic circulation. To the above reason, development of Piles favoured by constipation, prolonged standing, excessive straining at stool and Portal hypertension.

Hemorrhoids are classified into 2 types depending on their relation to anus. Internal Hemorrhoids lies inside the rectum and present with bright red rectal bleeding, when defecating. External hemorrhoids are under the skin around the anus, often result in pain and swelling in the anus. According to American society of colon and rectal surgeon is classified in grade I-IV of Hemorrhoid, Grade I is bleeding only, no prolapsed, Grade II: Prolapse that reduces spontaneously with or without bleeding, Grade III: Prolapse that require manual reduction, with or without bleeding, Grade IV: Irreducible prolapsed hemorrhoidal tissue.

The prevalence of Hemorrhoids ranges from 4.4% in the general population to 36.4% in general practice (Johanson et al 1990).The Prevalence of Hemorrhoids in India is about 40 million. It is now considered a major cause of morbidity and imposes burden on the society both economically and socially. Males and Females are affected with about equal frequency.

Best treatment is to advice Compatible diet and activities. Provided treatment should be easy to administer, free of any significant complication, reduces the likelihood of surgery, cost effective and easily available. Many Siddha classical preparations offers wide range of herbal, animal, mineral and herbo -mineral combination to manage Moolam successfully with minimum or no adverse effect. Siddha provide the best alternative management as it act on the root cause of diseases. In Gunapadam Moolikai, Nelli (Phyllanthus emblica, Linn-Euphorbiaceae) is indicated for the management of Rathamoolam. So, Nelli Kudineer is known for their activity in relieving symptoms of Rathamoolam. Pre clinical and Clinical trials are recommended to evaluate the efficacy and safety of Nelli Kudineer in patients suffering from RM and various factors related to RM also described in this study.

CHAPTER-II

AIM & OBJECTIVES

AIM OF THE STUDY

A Prospective Open labelled Phase II Non Randomized clinical study of Nelli Kudineer for Rathamoolam (Bleeding Hemorrhoid).

PRIMARY OBJECTIVE

- To evaluate the clinical and therapeutic efficacy of Nelli Kudineer for Rathamoolam.

SECONDARY OBJECTIVES

- To analyze Phytochemicals in Nelli Kudineer.
- To study the Pharmacological activities of the trial drug.
- To determine the biochemical contents of trial drug.
- To study anti microbial activity of the trial drug.
- To analysis the safety profile of trial drug through Toxicity study.
- To describe the panchbootha aspect of NK with its gunam for Rathamoolam.
- To record the aggrevating factors and prevalence of Rathamoolam.
- To perform the statistical analysis.

CHAPTER-III

REVIEW OF LITERATURE

III.1. NELLI DESCRIPTION

TAXONOMY (WIKIPEDIA)

Kindom : Plantae

Clade : Angiosperms

Clade: Eudicots

Clade: Rosids

Order: Malpighiales

Family: Phyllathaceae

Subfamily: Phyllanthoideae

Genus: Phyllanthus

Species: P.emblica

SYNONYMS

- *Cicca emblica* (L.) Kurz
- *Diasperus emblica* (L.) Kuntze
- *Dichelactina nodicaulis* Hance
- *Emblica arborea* Raf.
- *Emblica officinalis* Gaertn.
- *Phyllanthus glomeratus* Roxb.
- *Phyllanthus mairei* H.Lév.
- *Phyllanthus mimosifolius* Salisb.
- *Phyllanthus taxifolius* D.Don

Figure- III.1:Nelli parts

LEAF

ROOT

FRUIT

BARK

MACROSCOPIC APPEARENCE

Phyllanthus emblica L, Emblica officinalis Gaertn, Euphorbiaceae family, a small or medium sized tree, found in mixed deciduous forests. It grows in Kurinchi and Marutham Thinai.Small tree with hairy reddish brown branchlets. Greenish grey or red bark.Leaves several, subsessile,distichous.Flowers greenish yellow,in axillary fascicles.Disc absent in male.Berry greenish yellow,globose and fleshy. The seeds are trigonous.

Synonyms

Tam:Amalakam,korankam,Mirutupala,Datri

Eng:Emblic myrobalan

Mal:Nellikka

San:Amalaki,Amrithaphala,Dhathri

Chemical constituents

Fruits contain trigalloylglucose,terchebin,covilagin,ellagic acid,Phyllembic acid. Bark yields Leucodelphinidin,procyanidian,3-O-gallated prodelphinidin and tannin. The seed oil contain Vitamin C,carotene,Nicotinic acid,riboflavin,D-glucose,D-fructose,myoinositol,embicol,mucic ,phyllembic acid,phyllembin and fatty acid etc.Root, bark, Leaf, Flower, Fruit, Seed are used in diseases of Pitham, Coryza, Constipation,Fainting,Polyuria,Anemia,Ascitis,Piles,Dropsy, Hypertension, asthma, Tuberculosis and it is a Rejuvenator(Yoganarasimhan S.N, Medicinal plants of India Vol 2,2000&The siddha Pharmacopoeia of India,2008)

Described the Action: Fresh fruit is refrigerant, diuretic, laxative, carminative and stomachic. Dried fruit is sour and astringent. Flowers are cooling and aperint.Bark is astringent (Purushotam kaushik &Anil kumar Dhiman, Medicinal plants and raw drugs of India, 1999)

GUNAPADAM-MOOLIGAI

Variousnames:Aamalakam,Aalakam,Aambal,Aamarikam,thaaththaari,Thaaththiri,Korankam,miruthupala,Meethunthu.

Parts used: Leaf, Flower, Bark, Root, fruit, seed.

PROPERTIES AND ACTIONS OF NELLI

Table-III.1: Properties of Nelli

Taste(suvai)	Sour,Astringent,Sweet
Potency(Thanmai)	Cold
Post absorptive taste(Pirivu)	Sweet

Table-III.2: Actions of Nelli

Parts	**Action**
Leaf, bark,dried fruit	Astringent
Flower	Refrigerant,Laxative
Fruit	Refrigerant,Diuretic,Laxative

Pothu gunam

If nellikkai is taken in day time, following disease will cure.It is illustrated in **Theraiyar gunavakadam and Pathartha guna chinthaamani**

"பித்தமன லையம் பீனசனம்வாய்நீர் வாந்தி
மத்தமலக் காடும் மயக்கமுமில்-ஒத்தவுரு
வில்லிக்கா யம்மருங்கா மென்னாட்கா லந்தேர்ந்தே
நெல்லிகாயம் மருந்துண்".

The following disease will cure,

- Pitha noi
- Iya noi
- Peenisam
- Vaayneer
- Vaanthi
- Mayakkam

According to Theraiyar gunavakadam and Patharthaguna chinthaamani,

"நெல்லிக்காய்க்குப் பித்தம் நீங்கு மதன்புளிப்பால்
செல்லுமே வாதமதிற் சேர்துவரால்-சொல்லுமையம்
ஒடுமிதைச் சித்தத்தில் உன்ன அனலுடனே
கூடுபிற மேகமும் போங்கூறு."

Above poem revealed that nellikkai will cure

- Pitha diseases
- Vatha diseases
- Kapha diseases
- Diabetes

Root

According to **Agasthiyar Gunavakadam and Patharthaguna chinthaamani**, Root of nelli is used to cure following diseases.

- Vaanthi
- Agusea

- Normalizes Thirithodam
- Suram
- Sanni

“வமனம் அரோசியறும் வாதமுதன் மூன்றுஞ்
சமன முறுமலமுஞ் சாறும்-அமானசுரம்
புல்லிவரு தோடசன்னி பொல்லாச் செயலும் போம்
நெல்லிமர வேரை நினை”.

According to Theraiyar Yamaka venba

“இல்லாமலக மிரண்டு மயின்றானே
யில்லா மலகமிரிக்குமே-இல்லாமல்
வாழைக் கனியும் வடையு மிழுது முண்பான்
வாழைக் கனியுன் வைத்தவன்”.

Nellimulli

According to Theraiyar Gunavakadam and Patharthaguna chinthaamani, therapeutic uses of Nellimulli described

“ஆகவன லஞ்சசிஅ சிரிக்கென்பு ருக்கிகண்ணோய்
தாகமுதிரவித்தந் தாதுநஷ்டம்-மேகனத்தின்
இல்லிமுள்ளி போலருகல் எண்கா மியவியங்கம்
நெல்லிமுள்ளி யாற்போ நினை”.

- Eye diseases
- Thirst
- Blood loss
- Thathunattom
- Mega noi

According to Theraiyar gunavakadam and Patharthaguna chinthaamani,

“நல்லநெல்லி முள்ளியது நாக்குக் குருசிதரும்
அல்லல்விரி பித்தம் அதற்றுமதை-மெல்லத்
தலை முழுகக் கண்குளிருந் தாவுபித்த வாந்தி
இலையிழிமே கங்களும் போம் எண்”.

Nelli will cure following diseases

- It will give taste totongue
- Neutralizes the Pitham
- Coolinf to eye
- Pitha vaanthi
- Meganoi

In Patharthaguna chinthaamani,

மருள்சா ரடைகருணை வச்சிரவல்லி காட்டுக்

கருணை புளிநரளை காறாக்-கருணை

மெருகோடு வெள்ளறுகு வெண்சித்திர மூலம்

வரு மூலம் போக்கும் மருந்து.

Plants that cure piles are

- Marul
- Saaradai
- Karunai
- Vachiravalli
- Kaattukarunai
- Pulinaralai
- Karaa karunai
- Merugu
- Vellaruku
- Venchithiramoolam

III.2. JOURNAL PUBLICATIONS OF NELLI

Phytochemical and Acute toxicity study of Emblica

Pandey Govind and Pandey (2011) have done the work of Phytochemical and Acute toxicity study of Emblica officinalis, at the end of the study he found 250,500 and 1000 mg/BW of F.Albino rats,which showed LD50 for more than 1000mg/kg and further determined Hydro alcoholic extract of Emblica fruit showed the presence of Alkaloids,Glycosides,Tannins and Steroids.

Antibiotic activity of Emblica

Shubhi mehrotra et al.(2010)had determined the Antibiotic activity of Emblica ,it is effective against the three target pathogens,viz S.aureus,V.cholerae, and P.aeruginosa,Zone of Inhibition(ZIC) is 0.025,0.025and0.025(ug/ul)respectively

Anti cancer activity of Nelli

Gamkitidechakul N et al. (2010) have observed that the aquous extract of Amla containing Tannins (43%).Uronic acid (11%), and Gallic acid(21%) was effective in delaying and reducing DMBA induced and12-0-tetradecanoylphorbol-13-acetate-promoted skin carcinogenesis in mice.

Role in humoral immune response

Qari Muhammed Kaleem et al.(2014) studied on Emblica derived Tannins for their Immunostimulatory and protective activities againt Coccidiosis in Industrial Broiler Chicken.The study revealed that Tannins has vital role in humoral immune response in sheep red blood cells by haemagglutination assay($P \leq 0.005$)

Antiatherogenic, anticoagulant, hypolipidmic, antihypertensive, antioxidant, antiplatelet and vasodialatory effects

Fataneh Hashem et al.(2018) article reviewed the Emblica officinalis's(EO) potential for prevention and therapy of cardiovascular diseases. PubMed, ScienceDirect, Scopus, Proquest, Ebsco, Google, Ovid and Cochrane databases were searched from 1966 to 2017.Nineteen articles concerning the cardiovascular pharmacological effects of EO were included in this review. The plant has shown Antiatherogenic, anticoagulant, hypolipidmic, antihypertensive, antioxidant**,** antiplatelet and vasodialatory effects as well as lipid deposition inhibitory properties.

Plants having Antihemorrhoidal properties

Table-III.3: Plants having AntiHemorrhoidal properties Bharat Gami (2011)

Plant Name	**Chemical constituents**	**Family**	**Parts used**
Centella asiaticaL	Triterpen,saponin	Apiaceae	Whole plant
Aesculus hippocastanum L	Triterpen,saponin	Hippocatanaceae	Seeds
Ruscus aculeatus	Saponin,glycoside, ruscogenin	Liliaceae	Rhizomes
Hamamelis virginianaL	Tannins,Volatile oil	Hamamelidaceae	Bark
Gingko bilobaL	Bioflavanoid,Hesperidin	Ginkgoaceae	Leaves
Rosa canina	Vitamin C	Rosaceae	Fruits
Silybum marianum	Flavanolignans,silydisnin,silychristine, silymarin	Asteraceae	Fruits,seeds
Commiphora mukul	Diterpenoids	Burseraceae	Gum resin
Azadirachta indica	Sulphur containing bitter principle	Meliaceae	Seeds
Emblica officinalis	**Vitamin C,Tannin**	**Euphorbiaceae**	**Fruits**
Terminalia chebula	Tannin	Combretaceae	Fruits
Cassia fistula	Tannin	Caesalpinaceae	Pod
Calendula officinalisL	Salicylic acid	Asteraceae	Essential oil
Mimosa pudicaL	------	Fabaceae	Whole plant
Vitex negundo	Tannin	Verbenaceae	Whole plant
Eclipta alba	Alkaloids	Asteraceae	Whole plant
Plantago ovate	Mucilage	Plantaginaceae	Seeds
Collinsonia canedensis L	Flavanoids,saponins	Lamiaceae	--------
Matricariarecutita	--------	Asteraceae	Dried flower
Lupinus albus	VitaminC,Vitamin E	Fabaceae	--------
Vateria indica	Bitter resin	Dipterocarpaceae	---------
Mentha piperita	Pungent oil	Labiatae	Leaves
Aloe vera	Anthraquinone glycosides	Liliaceae	Dried juice of leaves
Cupressus sempervirens	-------	Cupressaceae	Twigs of young branches
Pelargonium graveolens	---------	Geraniaceae	Leaves and stems
Juniperus communis Linn	--------	Cupressaceae	Essential oil

Importance of Flavanoid in Hemorrhoid

Alonso et al. (2006**)** carried out the study regarding the flavonoid sand symptomatic Hemorrhoids. They reported, reduction in the risk of bleeding,persistent pain,Itching and reoccurrence. Recommended that more in-depth study with effective methodological quality needed for the apparent beneficial effects of flavonoid for the treatment of hemorrhoids.

Anti inflammatory and Dyslipidemic effect of Nelli

Antony B et al (2008) carried out a pilot clinical study to evaluate the effect of EO extract on markers of systemic inflammation and dyslipidemia. Purified, standardized, dried extract of amla containing about 35% galloellagi tannins along with other hydrolysable tannins were used for this trial . Their earlier studies on rabbits showed significant reduction in total cholesterol and triglycerides as well as increase in HDL. This study extends these results to human volunteers. Two doses of the extract were evaluated 500 mg and 1000 mg per day for 6 months. Blood samples were collected at the 3rd and 6th months showed reduction in total and LDL cholesterols and enhancement of beneficial HDL cholesterol. In addition, blood CRP levels, a marker for inflammation, were also significantly reduced.

Antioxidant action of Emblica

Renuka Chaphalkar et al. (2017) conducted a study on Antioxidants of Phyllanthus emblica bark extract (PEE) provide hepato protection against Ethanol induced Hepatic damage. They investigated the protective effect of the hydroalcoholic extract of *Phyllanthus emblica* bark (PEE) in ethanol-induced hepatotoxicity model in rats. Total phenolic, flavonoid, and tannin content and in vitro antioxidant activities were determined by using H_2O_2 scavenging and ABTS decolorization assays. This result showed that PEE was rich in total phenols (99.523 ± 1.91 mg GAE/g), total flavonoids (389.33 ± 1.25 mg quercetin hydrate/g), and total tannins (310 ± 0.21 mg catechin/g), which clearly support its strong antioxidant potential. HPTLC-based quantitative analysis revealed the presence of the potent antioxidants gallic acid (25.05 mg/g) and ellagic acid (13.31 mg/g). Moreover, one-month PEE treatment (500 and 1000 mg/kg, p.o.) followed by 30-day 70% ethanol (10 mL/kg) administration showed hepatoprotection as evidenced by significant restoration of ALT ($p < 0.01$), AST ($p < 0.001$), ALP ($p < 0.05$), and ATP ($p < 0.001$) and further confirmed by liver

histopathology. PEE-mediated hepatoprotection could be due to its free radical scavenging and antioxidant activity that may be ascribed to its antioxidant components, namely, ellagic acid and gallic acid.

Action of Nelli on Vascular smooth muscle

Junxuan Zhou et a.l(2018) their study illustrated that Emblic leaf flower fruits ameliorate vascular smooth muscle cell dysfunction in hyperglycemia, an underlying mechanism involved in Ellagitannin metabolite Urolithin A. In this study, acetylcholine-induced endothelium-independent relaxation in aortas was facilitated upon emblic leaf flower fruit consumption in the single dose streptozotocin-induced hyperglycemic rats. Emblic leaf flower fruit consumption also suppressed the phosphorylation of Akt (Thr308) in the hyperglycemic aortas. More importantly, urolithin A (UroA) and its derived phase II metabolites were identified as the metabolites upon emblic leaf flower fruit consumption by HPLC-ESI-Q-TOF-MS. Moreover, UroA reduced the protein expressions of phosphor-Akt (Thr308) and *β*-catenin in a high glucose-induced A7r5 vascular smooth muscle cell proliferation model. Furthermore, accumulation of *β*-catenin protein and activation of Wnt signaling in LiCl-triggered A7r5 cells were also ameliorated by UroA treatment. In conclusion, their data demonstrated that emblic leaf flower fruit consumption facilitates the vascular function in hyperglycemic rats by regulating Akt/*β*-catenin signaling, and the effects are potentially mediated by the ellagitannin metabolite urolithin A.

III.3. SIDDHA LITERATURE REVIEW OF RATHAMOOLAM

Rathamoolam is one among the twenty one types of Moolanoikal, described by Yugimuni. Moolam in Siddha means the area of Moolaatharam or the Root. A disease associated with Moolathara region is Moolarogam or Anorectal diseases.They are also called Adimulai noi, Arippu noi , Eruvaimulai noi and Mulai noikal.

IMPORTANCE OF MOOLAATHARAM

According to **Chattamuni jnanam** Moolathara area has been given importance in Siddha systems as it is the energy center of the body, the Kundalini. The Chattaimuni jnanam verses tell about the importance of moolathara among six aathaarams. So, according to chatta muni, moolaatharam is a vital role of the disease.

“பாங்கானகுண்டலிக்குள்மூலமொன்று
பாரப்பாகண்டத்தில்மூலமொன்று
போங்கானபுருவமையமூலமொன்று
புகழானவிந்துவிலேமூலமொன்று…”.

UDAL KOORUKAL

The total length of the GIT is thirty two muzham and the spindle like shape of the intestine occurring during peristalsis and the taeniae in the large intestine are known as ‘Arai’. These are 1008 in number. They look like kumizhi, ie.bubble like masses in a long tunnel. These structures are controlled by the six chakras and the guru naadi. In the moolathara area the large intestine is to function normally in association with other systems in the region particularly related to vaayus vairavan and sanguni.

“கூறவேமுப்பத்திரண்டுமுழம்குடல்தானும்
முறையாகஆயிரத்திஎட்டுஅறையுமாகும்
அறையென்றால்நுரையதுபோல்குமிழியாக
அடைவாடிநிற்க்குமெடாகுடலில்தானும்
கம்பத்திலறைடிட்டாப்போலேயந்த
கருங்குடலில்இதனளவும்ஆயிரத்திஎட்டு
ஆதாரம்ஆறுக்கும்குருநாடிக்கும்
அறைஅறையாய்குடலணைபோல்நின்று
அறையாகஇடப்பக்கம்சலப்பைக்குள்ளே
வலப்பாகம்குடல்நாளம்சங்கினோடே
வைரவனும்சங்கினியும்அங்கேநின்று
வளர்க்குமடாசங்கதையும்உறவாடிசுழியில்வந்து
அங்குநிர்க்கும்மூலத்தில்குழல்தானென்றே
ஒளியானஅக்குழல்தானறையும்பூட்டி
கதவில்தாப்பாளிட்டாப்போலடைப்பாப்போல்
அடவாகஅதன்வழியாய்மலம்தான்போகும்
…….கருவிபாசம்”.

Nine narambukal are held responsible for deglutition, digestion, absorption and defaecation. Out of these, one narambu is responsible for the purpose of visarkkam. The narambu divides into four branches in the moolatharam and supplies large intestine, urinary bladder, sukkilasayam, kaariral and suvaasapai. This narambu in association with other thathuvams such as ten vayus carryout the act of visarkkam.

“காணும்முப்பத்திரண்டுமுழம்தானும்
மூலாதாரத்தில்இதழொன்றாய்நாலும்சென்று
சோறானஓரிதழ்தான்சுக்கிலதில்சென்று
சென்றுமலசலாதிகளைதள்ளிப்போடும்
பொறியானமூன்றிதழும்பவளப்பையில்
சேர்ந்துமுதுக்கிணையதுபோல்இரைகள்சூழ்ந்து
கொண்டாடிஅங்கிருக்கும்இதழ்மூன்றாலே
ஒன்றானகுடல்நரம்புதிரளாய்நின்று
ஊக்கமுள்ளகாரீரல்தன்னில்தாமரை
நூல்வளையம்போல்மோதிநிர்க்கும்
நிர்க்குமந்தநரம்பதுவும்சுவாசப்பையில்
தண்டதுக்கும்உறவாச்சுமலத்தைப்போக்கும்
பேரானதசவாயுவின்பெலத்தாலே
இழுத்துத்தள்ளுமடாமலத்தைதானே”

UDAL THATHUVAM

Moolathara is situated in the akkini manadalam and vatha area is below the navel. Predominent bhoothams are Vaayu Theyu and Akaayam. Theyu is for akkini mandalam and the rest for vatha area. This structure makes this area having more kinetic (due to vaayu) and thermal energies (due to theyu) to facilitate the normal act of micturition, defaecation and parturition. To control defaecation and to carry out (kanmavidayam) visarkkam, the bootham involved is neer. The kanmenthiriyam involved here is Eruvai.

Vaayu and Akayam together constitute Vatham.Vatham in the body manifests as 10 types. The types directly concerned with moolathara area are Abanan,Pranan and Devathathan. Abanan is a vaayu having theyu predominance in its structure. In relation to malasayam it effectively expels faeces. Prana vaayu takes its course via moolathara area and it takes saaram from here and disperses to all tissues of the body in addition to its main function of respiration. Devathathan relates the mental states of the human body due to Rathamoolam. It normally resides in the rectum and is responsible for anxiety, anger, quarelling and laziness. Theyu in malaasayam manifest as moolakkini. Moolakkini is a kind of akkini in the body gives the required metabolic thermal energy to malasayam to facilitate the normal act of visarkkam. Neer bootham carries out the act of visarkkam in the kanmenthiriyam Eruvai. The

action of neer bootham is very essential, but uncontrolled action by vaayu, akayam and theyu leads to decrease in Neer bootham and may result in pathology.

According to **Theraiyar narambu soothiram** 150, In the ten naadis, the malasaya naadi is Guku. Suzhumunai naadi also has its base in the moolatharam. These naadis carryout coherent action of other systems in normal act of digestion, absorption and defecation.

"தேறவென்றால்குகுவென்றநரம்புதானும்
செயலாகமுன்சொன்னமுக்கோணில்நின்று
கொனாகும்அங்குநின்றுநார்போலே
கொடுமையடாஅந்நரம்புமேல்போட்டாக
அபானத்தில்முன்னாளவாய்அங்கேநிற்க்கும்
காருதிகம்உளப்பைநரம்பிதாமே
தானென்றநரம்பெல்லாம்இசைவாக
துண்டுபோல்தேகத்துள்ளே
அன்னமதுஉண்பதற்கும்தெகிப்பதற்கும்"

TYPES OF MOOLAM (NOI ENN)

Yugi vaidhya chinthamani (21 types)	**Cegaraasasekaram (20 types)**	**Theraiyar (10 types)**	**Agathiyar paripooranam (9 types)**	**Anubava vaidhya ragasiyam (6 types)**	**Jeeva ratchamirthan (4 types)**
Neer Chendu Mulai Siru Varal **Ratha** Seezh Aazhi Thamaraka Vali Azhal Iya Thontha Vinai Mega Pavuthira Kiranthi Kutha Pura Churukku Chavvu	Vatha Pitha Kapa Vatha Pitha Pitha Vatha Pitha Kapa Setha Vatha Sada Vatha Kapa Sala Ul Ulaththu Athisara sura Thosha thontha Vatha raththa Vatha Kerppa Pitha Vatha Thontha Pitha Kapa Thontha Kanda **Ratha** Serpa	Seezh Punn Thee Neer Mulai Sathai Kaduppu Veluppu Kaatru Perumulai	**Ratha** Seezh Mulai Moola paandu Vali Azhal Iya Ul Pura	Vatha Pitha Kapa Thontha Thirithoda **Ratha.**	Sagasa (hereditary) Uththarasa (natural) Shutka (shrinking) Aarthira (discharge)

Yugi vaidhya chinthamani -800(Stanza 639-669)

தானானமூலமதுஇருபத்தொன்றும்
சதாசிவன்றான்பராபரியாட்கருளிச்செய்ய
பானானபராபரியான்நந்திதேவர்க்குப்
பாஷிக்கநந்திதன்வந்திரிக்குச்சொல்ல
கோனானதன்வந்திரிஅசுவினிக்குஞ்சொல்லக்
குணமானஅசுவினியும்அகத்தியருக்குச்சொல்ல
ஆனானஅகத்தியரும்புலத்தியருக்குச்சொல்ல
அவர்தானேதேரையருக்கருள்செய்தாரே.

"சனிப்பானமூலத்தின்பெயரேதென்னில்
சமரசமாம்நீர்மூலஞ்செண்டுமூலம்
முனிப்பானமுளைமூலம்சிற்றுமூலம்
மூர்க்கமாம்வறண்மூலம்ரத்தமூலம்
தினிப்பானகீமூலம்ஆழிமூலம்
திணியானதமரகமாமூலத்தோடு
வனிப்பானவாதமொருபித்தமூலம்
வகையானசிலேட்டுமத்தின்மூலமாமே**.**
வகையாருந்தொந்தமாமூலத்தோடு
வளர்கின்றவினைமூலமேகமூலம்
பகையாகும்கும்பவுத்திரமாமூலத்தோடு
படர்கிரந்திமூலத்தோடுகுதமாமூலம்
பகையாகும்புறமூலஞ்சருக்குமூலம்
பொருகின்றசவ்வாகுமூலத்தோடு
தகையாகமூலமதுஇருபத்தொன்று
தண்மையாய்ச்சுற்றியதினசுரூபந்தானே**."**

Agasthiyar rathina churukkam naadi nool

வேலிநோய் படுவதிலே நாற்பத்தாறு
வெகுமூல மொன்பதாங் கழல் நோய் பத்தே**.**

The above literature explained,diseases are classified as 4448 in numbers. Moola rogam is of nine types

ETIOLOGY (NOI VARUM VAZHI)

Primary cause of Moolanoi

Accoding to **Theriyar** concept,

"அனில பித்த தொந்தமலாது மூலம் வராது"

"கபமான நீரதுவுமின்றி சோபை வராது"

Rathamoolam Initially from derangement of Vatham and Pitham.Initially in any pathological state the affected Thathuvams are the Panchabootham.The various etiological factors deranges the normal structure of Vayu, Akayam and Thee bootham in the Moolatharam.If this state is allowed to persist then the bootham responsible to carryout kanmavidayam visarkkam, Neer get deranged in the very long run.Since Vayu and Akayam constitute Vatham and Thee constitute Pitham,immediately these two humours derange.

Vatham in the body manifests as 10 vayus,among them those having connection with the Anal canal is Abanan,Pranan and Devathathan get deranged.Simultaneously with vayus,Naadi is having connection with Moolatharam i.e.Guku and Suzhumunai along with other Thathuvams produce systemic manifestations. Pitham in the body manifests as 5types viz Anal, Ranjakam, Prasakam, Alosakam and Saathakam. All these are affected in Rathamoolam. Kapam deranges very lately, if left untreated and will cause sobai noi.

According to **Yugimuni,**

“தத்தையாமதிகமாங்குளிரினாலும்
தரியாதவழ்ற்சியால்கிரந்தியாலும்
புத்தையாம்பொருந்தாதஉஷ்ணத்தாலும்
புணர்ச்சியாற்கோபத்தார்சலிப்பினாலும்
கத்தையாம்வெகுகாரம்வெண்டலாலும்
கடினமாம்உப்பாலும்காரத்தாலும்
மொத்தையாம்வெகுதனங்கள்போனதாலும்
மூலம்வந்துற்பத்திமுனையுந்தானே”.

The above poem was mentioned the following characteristic intrinsic causes of Incompatible diet and acts include,

- Exposure to excessive cold
- Exposure to excessive heat
- Excessive heat in the body due to Kiranthi noigal (STD)
- Indulging excessively in sexual activities
- Excess intake of Pungent and Salt diet.

“முனையாகமூத்தோரைவைதலாலும்
மோசங்கள்பண்ணியேகற்பழித்தும்
நினைவாகநினைவிலொன்றும்வாக்கிலொன்றும்
நேர்ந்தபடிசொல்லுகின்றநீட்டுநற்க்கும்
பனையாகபரதேசிபந்துவானோர்
பசித்திருக்கஉன்டதோர்பாதகர்க்கும்
தனையாகச்சமாதானந்தவிக்கின்றோர்க்கும்
சன்டானமூலம்வந்துசனிக்குந்தானே.”

The following karmic activites can causes for the disease, including

- Chiding the elders
- Doing harm to others
- Indulging in rape
- Thinking of doing harm in the mind but saying sweet words in front
- Living a luxurious life when others are in hunger
- Quarrelling with others

Psychological cause described is,

- Angry
- Anxiety and Depression

Other Causes

- Maintaining wrong Yogic postures
- Predispose to vitiated Vatham, Pitham and Moolakkini leading to Moola noi.

According to **Subramani varama avathinithanam-500**, was described the etiology due to deranged varma nilai.

“நேரான நெற்றி நடுவதிலிருந்து
அவரவர் கையதினால் எட்டு விரல் மேலே
அளந்து பாற்த்தால் தலமுனக்கு தெரியவரும்
அத்தலத்தில் முறிந்திடிலோ குணத்தைக் கேளே
மேல் மலர்ந்து வலிக்குமப்பா வயர் பொருமும்
பொருமியே சிறுனீரொடு பேதி கட்டும்
கழ்ட்டமப்பா சன்னியோடு சீதமுண்டாம்
தப்பாது நாழிகைதான் அறுவதுக்குள்….”.

Agasthiyar gunavakada thirattu, Pathinen siddhar aruli chaitha naadi, Athamaratchamiritham, Agasthiyar-12000 described the etiology of Rathamoolam,

“மூல மிறைச்சி தானு முதிரவே தின்கையாலும்
பாலு டனினிய கண்டில் பரத்துடன் திங்கையாலும்

சால நெய் புசிக்கையாலுந் தையலார் வேட்டையாலு
மாலகேர் விழியினாளே ஆகிய வரட்சியாமே
வேகமாந் திரவியங்கள் மிகுகையால் நூற்கையாலும்
சாகமாங் கொமட்டிக் காய்தான உன்கையாலும்
காசிய பன்றி மாங்கிஷம் கடுந்தினி துன்கையாலும்
நீதியிற்றறியே தோங்கி நிரந்தர மிருகையாலு
போதிய பகற்கண் தூங்கி யுயர்ந்திடு மூலந்தானே
காயத்தில் மூலரோகங் கண்டிடும் விதங்கள் கேளாய்
பாயயொத்த தீபனம் பசியை யடக்கில் வாயு
மாயத் திலிருந்திக் கொண்டு மலவறை யடைக்கும் போது
ஓயத்த குண்டலிக்குட் புகும் வாயு தானே
வாயு புகுந்து மலத்தோ டபானத்தை
தேயுவை கூட்டி திரட்டி சுருக்கிடும்
தோயு மலம்வரின் சுருக்கி முன்னே
நின்ரேயு முளை போல பானனிருக்கும்"

(Agathiyar 2000)

- Excess intake of Non-veg foods
- Excess intake of fatty substances
- Hunting
- Intake of Kummattikkai
- Intake Pig meat
- Sleep in day time
- Supression of hunger

PATHOGENISIS

Noi naadal Noi muthal naadal thirattu I describes the Pathology of Moolam.It basically result from derangement of Vatham and Pitham. Initially in any pathologic state the affected thathuvams are the Panchabootham, The various etiological factors of Ratha moolam deranges the normal structure of Vaayu,akayam and Thee bootham in moolatharam, if this state is allowed to persist then the bootham responsible to carryout the kanmenthiriyam visarkkam,neer gets deranged in the very long run,since vaayu and akayam constitute Vatham and Thee constitute Pitham,immediately these two humours deranged. Vatham in the body manifests as 10 vaayus. Among them those having connection with the anal canal is Abanan, Piranan and Devathathan get deranged. At the same time Naadis having connections with the moolatharam is Guku and suzhumunai along with other thatuvams produce systemic manifestations. Pitham

in the body manifests as Five types viz Anal, Ranjakam, Prasakam, Alosakam and Saathakam. All these are affected in Rathamoolam. Kapam deranges very late stage if the patient is left untreated for longer duration and causes sobai.

In Rathamollam primarily affected vaayus are Abanan, Pranan and Devathathan. These deranged vaayus affect seven thathus and Malams. Due to this symptoms produced in rathamoolam are Pain in and around umbilicus, splashing of blood during defaecation, weakness, and headache. Pain in umbilicus and Splashing of blood during daefaecation are symptoms of affected abanan. Feeling of weekness in the limbs, headache is the characteristic features of pranan involvement. Devathathan produces anxiety due to loss of blood.

As molatharam is in the akkini mandalam, any pathological condition here can harm moolakkini and eventually Pitham. In Rathamoolam, all the Pithams are affected except Analpitham initiallay. Later when Veluppu noi ensues, it gets also affected leading to reduced appetite. The primarily deranged Pithams are Ranjaka, Prasaka, Aalosaka, Saathaka pitham. Symptoms are produced when these deranged pithams affect the seven thathus and malam. These symptoms include Pale skin, Veluppu noi, yellow colour eye,giddiness and emaciation. Veluppu is due to derangement of ranjakam. Paleness of skin is due to derangement of prasakam, yellow colour eye is due to derangement of Alosakam, giddiness and emaciation are due to derangement of sathakam.

Kapam has neer and Prithvi boothams.It is responsible for coordination and defense mechanism of the body. Initially in Rathamoolam, kapam is not deranged but in untreated cases all the five types of kapam are affected. This causes pathologic changes in the thathus leading to sobai noi.When Vatham, Pitham and kapam are deranged, they affect udal thathus(saram,senneer,oon,kozhuppu,enbu,moolai,sukilam or suronitham) and udalthee. It will afeect three malams and intern produce various symptoms according to severity and site of ailment.

In Rathamoolam primarily affected thathus are saram, senneer and oon.The symptoms of Rathamoolam are typically due to vitiation of these thathus. In udalthee, moolakkini is affected.Moolakkini along with abaanan causes bleeding per anus which is the main symptoms. Due to malam derangement constipation, Irritation around anus results.

Thirumolar karukkidai vaidhyam-600 mentioned the Pathology of RM

"காயத்தில் மூலங்கண்ட விதங்கேளு
பாயொத்த தீபனம் பரிந்தே யடக்கினும்
மாயை மயக்க மலத்தை யடக்கினும்
ஒயுற்ற குண்டலிக்குள் புகும் வாயுவே
வாயு புகுந்து மலத்தோட பானத்தை
தேயுவைக் கூட்டித் திரட்டி சுருக்கிடும்
தேயும் மலம் வரின் சுருக்கி முன்னே
நின்றேயு முளை போலபானனிரிக்குமே
இரிக்குஞ் சிலமூல மெழு மன்டலம் போல
மறுக்கரணம் கொண்டு வருஞ்சில மூலம்
உறுக்கிய வாயுவா லுதிரம் தான் கூடித்
தறுக்கி விழுக்காட்டும் தான் **ரெத்த மூலமே**".

Describes the pathology of Rathamoolam in above poem is. The Suppression of appetite and defaecation leads to derangement of vayu.This vayu enters kundalini area.Here the vayu combines with theyu and causes formation of moolamulaikal.When excess vayu exerts pressure on them,they bleed on straining ie,while defaecation

CLINICAL FEATURS (KURI GUNANKAL)

According to the **Yugi munivar in chinthamani**, poem no 650 is,

"சேதியாய்தொப்புள்தன்னில்வலித்துநொந்து
சிறுகதிர்போற்பீறிட்டுரத்தம்வீழும்
மேதியாய்மேனிவற்றிவெலுத்துப்போகும்
மிகைகாலசந்துமேசோகையாகும்
மாதியாய்மார்பிளக்கும்தலைநோவுண்டாம்
மயக்கந்தான்மிகுதியாய்தள்ளிப்போகும்
நாதியாய்க்கண்ணிரண்டுமஞ்சள்போலாம்
நலியும்ரத்தமூலத்தின்பண்புதானே".

- Pain around umbilicus
- Bleeding per anus
- Emaciation of body
- Pallor
- Weakness of extrimities
- Sogai

- Chest pain
- Headache
- Mayakkam
- Yellowish eye.

According to **Agathiyar gunavakadam**, mentioned the clinical features,prognosis and symptomatic treatment in Rakthamoola noi.

தானான ரத்தமூலம் சொல்லக்கேளு
தனியான உள்மூலம் தன்னில் நின்று
தேனாக வருகின்ற ரத்தமப்பா
தெளிவாக நாளத்தில் நின்று தானும்
ஊனான நாடி தனில் இருந்து எழும்
உள்ளபடி தோன்றுமடா ரத்தந்தானும்
மானான இதுதீர வகையைக் கேளு
மக்களுக்குச் சொல்லுகிறேன் மகிழ்ந்து கேளே.
கேளடா ரத்தந்தான் நிதமாயப்பா
கெணிதமுடன் நாள்தோறும் கண்டாலுந்தான்
நாளடா துர்பலமா யிருந்தாலுந் தான்
நலமான தலைவலியு மடைந்தாலுந் தான்
தேளடா இதற்கொரு உபாயங்கேளு
தெளிவான ரத்ததை நிறுத்தாமல் தான்
நாளடா உலகத்துப்படி செய்து கொண்டு
நலமான பொசனந்தான் செய்து வையே.
செய்த பின்பு லகுவாக பேதிக் கீய்ந்து
செயலான ரோகத்தைப் பொகச் செய்வாய்
உய்க்கின்ற ரோகிக்கு துர்பலமே கண்டு
உதடு வெள்ளை நாடியுந்தான் மெலின மாகில்
பெய்கின்றரத்ததை நிருத்திப் பின்பு
பிலமான மாசிக்காய் கஷாயத்தை
நையவே ஆசனத்தி லடித்தா யானால்
நன்மையுள்ள ரத்தந்தான் மாறிப் போமே.

According to the above poem the predominant symptoms of this diseases includes protrusion of tortured pile mass followed by anal bleeding, fatigue, and headache. In this condition nutritious diet which is laxative should be given to the patient. When the patients developed the symptoms of dehydration like pallor in the lips, feeble pulse peechu should given with the decoction prepared by Masikkai which

has styptic action will arrest the bleeding. Clinical features are presence of pile mass, Swelling of pile mass, bleeding per rectum.

According to **Sekharasa Kesaram** clinical features are described by below verses

"இருக்கும் சில மூல மெழு மண்டலம் போல
மறுக் கரணங்கொண்டு வளருஞ் சிலமூலம்
முறுக்கிய வாயுவால் உதிரந்தான் கூட்டித்
தருக்கி விழக் காட்டுந்தான் **ரத்தமூலமே**"

From **Thirumoolar Karukkidai Vaidhyam-600** clinical features described as

"மூலமே யெழுந்தபோது மூலத்தில் கனல் தான் மீறும்
மூலமே யெழுந்தபோது முனைவிந்து நாசமாகும்
மூலமே யெழுந்த்போது முழங்கவே யிரைச்சலாகும்
மூலமே யெழுந்த்போது முகிலில்லாக் கழிச்சல் தானே".

The above poem reveled the clinical features of Moolam.i.e. Burning sensation in anus, derangement of Vinthu, Iraichal(gurgling)and Diarrhoea.

In **Siddha maruthuvam pothu,** Murkuri gunam (Premonitory symptoms) described

"காணப்பா வாயுவாலும் கனத்த வபானன் றன்னைப்
பூணப்பா மலத்தைக் கட்டிப் புகையெனக் கறுக்கி நாளும்
தோணப்பா முளையைப் போலச் சுருக்கிமுன் மலந்தான் வீழல்
ஆணப்பா வபானந் தன்னை அழ்த்தவே இருக்கும் பாரே".

"மூலமே யெழுந்தபோது மூலத்தில் கனல் தான் மீறும்
மூலமே யெழுந்தபோது முனைவிந்து நாசமாகும்
மூலமே யெழுந்த்போது முழங்கவே யிரைச்சலாகும்
மூலமே யெழுந்த்போது முகிலில்லாக் கழிச்சல் தானே".

Premonitory symptoms are

- Constipation
- Protrusion of pilemass
- Burning sensation in anus
- Derangement of Vinthu
- Iraichal

According to **Theraiyar sekarappa,** Pothukuri gunangal (Clinical features)as

"மலமிறுகித் தழையுமேயுஞ் சுவேத மையின்
வகைமை யெனக் குழல்கடைத் தாமரைப் போல்
பலமிதமா யொருவேளை யபானஞ் சுற்றிப்
பதும முகிழ் விரியமைதிப் பிரசம் போலச்
சலசலெனப் பொசி குருதித் தில்லை பொங்கத்
தள்ளாடி வசமழியத் தளர்வுண்டாக்கி
நிலவரமற் றிடவஞரை யுஞற்று மையா
நீசத்துவ மூல குணத்தை
யென் சொல்வேன் பாந்தளிடியினி லொடுங்கு மாறே
யெவரையுங் கசங்கச் செய்து குடி கெடுமாறு செய்யுங்
கொண்டவநாயும் கெய்து.....நூலோர்"

The Pothu kuri gunankal(clinical features)as Faeces become hard and white in color and their passage in the anus gets blocked as if there is bud of lotus.Then the pile mass protrudes like a lotus flower with the active play of vayu.Bleeding per anus occurs like honey drops from the lotus flower.Malaise, Physical and mental fatigue also will develop.This disease is an irritating and the affected person looks like an afraid serpent due to heavy thunder.

In the literature **Gunavakadam**, Clinical features described are

"தொப்புளும் வலிந்து நொந்து துளங்கிடா யிரத்தம் வீழ்ந்து
அப்பொழுதுள்ள மூலமறியவே வெளியில் தள்ளும்
தப்பிடா மேனிவற்றித் தறுகிடா தூடே சென்று
இப்படி ***ரத்தமூல*** *மொன்றுதா னியமபலாமே".*

- Pain around the umbilicus
- Bleeding from rectum
- Prolapsed rectal mass
- Secondary anemia due to bleeding

Aaviyalikkum amuthamurai churukkam:

The above book was mentioned the clinical features of Hemorrhoids

- Loss of appetite
- Lower abdominal discomfort
- Constipation
- Pain around umbilicus

- Bleeding per anus
- Drowsiness
- Anaemia
- Breathlessness

Athmaratchamirtham entra vaidhya saara sangirakam

The above book was described the following clinical features are,

- Consuming food with bitter and sour tastes
- Warm body
- Loss of appetite
- Lower abdominal discomfort
- Constipation
- Pain around umbilicus
- Bleeding per rectum
- Protrusion of pile mass
- Irritation and burning sensation in the anus
- Anaemia

Veerama munivar aruli cheytha nasakanda venba

The clinical features are,

- Pain in the Umblicus
- Spurting out of blood during defaecation
- Emaciation
- Pallor
- Weakness in limbs
- Sobai
- Chest pain
- Headache
- Giddiness

PROGNOSIS (SAATHIYAM / ASAATHIYAM)

Saathiya Moolanoikal (Curable types)

தானென்ற மூலத்தி லசாத்தி யந்தான்
சாதகமாய் நீர்மூல முளை மூலந்தான்
*வானென்ற வறள்மூலம் **இரத்த மூலம்***
வாதமா மூலந்தான் பித்தமூலம்
வேனென்ற மேகமா மூலத்தோடு
விளை பவுத்ரமூலமாங் கிரந்தி மூலம்
பேனென்ற புறமூலஞ் சுருக்கு மூலம்
பெருகு சவ்வுமூலம துசாத்ய மாமே.

-Yugi

1. Neer moolam
2. Mulai moolam
3. Varal moolam
4. Rathamoolam
5. Vatha moolam
6. Pitha moolam
7. Mega moolam
8. Pavuthira moolam
9. Kiranthi moolam
10. Pura moolam
11. Churukku moolam
12. Chavvu moolam

Asaathiya Moolanoikal (Incurable types)

ஆமென்ற வசாத்தியத்தைச் சொல்லக் கேளாய்
அழிவு செண்டு மூலமாஞ் சிற்று மூலம்
தேமென்ற சீமூல மாழி மூலம்
திணிவான தமரகமா மூலத்தோடு
வேமென்ற வினைமூலஞ் சேட்பமூலம்
மிளிர்கின்ற குதை மூலந் தொந்த மூலம்
ஒமென்ற ஒன்பதும சாத்தியந்தான்
உறுதியாய் மூலத்தி னுண்மை தானே.

-Yugi

1. Chendu moolam
2. Sitru moolam
3. Seezh moolam
4. Aazhi moolam
5. Thamaraka moolam
6. Vinai moolam
7. Silethuma moolam
8. Kutha moola
9. Thontha moolam.

NAADI NADAI IN RATHAMOOLAM

According to **Theraiyar**, Primary Naadi in Rathamoolam is Pitham

அனில பித்த தொந்தமலாது மூலம் வராது

Vallathi naadi

Pithathil vatham is the diagnostic naadi for moolanoikal

“வண்ணமுடன் பித்ததில் வாதம் வந்தால்
வருமாறு பீனிசங்கள் மண்டைக் குத்து
கண்ணுமடாபவுத்திரங்க ளரையாப்புண்டாந்
தப்பாது நவமூலஞ் சாருந்தானே”.

-வல்லாதி நாடி

Sathaka naadi

Describes the pathological naadi for Moola noi

“வாதமெனும் நாடியது தோன்றில்
சீதமந்தமொடு வயிறு பொருமல் திரட்சி வாயு
சீதமுறுங் கிராணி மகோதரம் நீராமை
திரள் வாய்வு சூலைவலி கடுப்புத்தீரை
நீதமுறுங் கிருமி குன்மம் அண்டவாதம்
நிலையும் நீர்க்கிரிச் சரங்கள் தந்துமேகம்
பேதகமா முதரப் பிணி ***மூலரோகம்***
பேசவெகு பிணிகளுமே பொருளதாமே”.

-சதக நாடி.

சிறப்பன பித்ததில் வாத நாடி
சேரிலுறு தாதுநட்ட முதரப் பீடை
உறைப்பாகச் செரியாமைக் குன்மஞ்ச் சூலை
உற்றசுரங் கிராணி வயிற்றிரைச்சல் மந்தம்
அறைப்பன ஒங்கார புறநீர்க் கொவை
ஆயாச மிரக்கமொடு மயக்க மூர்ச்சை
*முறைக்காய்வு விஷவீக்கம் **மூலவாய்வு***
முரடான நோய்பலவு முடுகும் பண்பே.

Gunavakada noin saaram

Vatham,Pitham and Kapam are decreased from their normal state in Moolam "மூவரு மந்தமானால் முளைந்திடு மூலமெல்லாம்".

DIAGNOSIS (PINIYARAI MURAI)

Diagnosis by Porial Arithal, Pulanal therthal, Vinathal, which include detailed history of patient and Envagaithervukal, which include Naadi,Sparisam,Naa, Niram, Mozhi, Vizhi, Malam and Moothiram

DIFFERENTIAL DIAGNOSIS (NOI KANIPPU VIVAATHAM)

- Chendu moolam
- Muli moolam
- Varal moolam
- Aazhi moolam
- Thamaraka moolam
- Azhal moolam
- Churukku moolam
- Rathasoolai moolam
- Vazhi kuruthi azhal noi

COMPLICATIONS

When moolakhni is highly vitiated it will cause worst complications according to Thiruvalluva Nayanar Navarathna Chinthamani-800. The main complications are veluppu noi due to deranged azhal and sobai due to deranged iyam which mentioned in Yugi Vaidhya Chinthamani. Moolam accompanied by edema of extremities, abdomen, face, anal region and umbilicus results in death. If moolam come as a complication of Magotharam and preliminary disease of paandu, kaamalai, gunmam

and kazhichal will cause more complications. If moolam accompanied by Kudhakeelam they felt intolerable pain.

LINE OF TREATMENT

- Administration of internal medicine to normalize the Vatham&Pitham and to reduce the vitiated moolakkini. And medicines to stop bleeding, to reduce inflammation and to relive constipation.
- Pathiyam, i.e. diet to normalize the vitiated vatha pitha thontham and to maintain the effectiveness of drug.
- Yoga therapy and pranayama therapy to normalize the bowel habit and mukkutram.

PATHIYAM FOR RATHAMOOLAM (DIET)

Anubava vaidhya deva ragasiyam prescribed the following diet regimen

- Cows buttermilk
- Cows butter
- Cows ghee
- Pepper
- Asafoetida
- Rock salts
- Tender mango
- Caster oil
- Fresh green such as araikeerai, siru keerai, thuthulai keerai, venthaya keerai, manathakkali keerai, mullanki keerai.

APATHIYAM (DIET RESTRICTION)

- Fish
- Meat
- Black gram
- Ragi
- Rye
- Bitter guard
- Maize
- Oil cake of eluppai
- Hot foods and drinks
- Motchi
- Brinjal

III.4. MODERN ASPECT OF RATHAMOOLAM

DEFINITION

Hemorrhoids are dilated veins occurring in relation to the anus.

TYPES

1. Internal hemorrhoids: saccular dilatations of internal rectal venous plexus, occur above the pectinate line. Bleed profusely during straining at stool.
2. External piles: it occur below the pectinate line

ETIOLOGY

1. Poor support to veins the surrounding loose connective tissue
2. Absence of valves in superior rectal and portal vein
3. Compression of the veins at the sites where they pierce the muscular coat of the rectum
4. Direct transmission of the increased portal pressure at the portosystemic communications

For the above reason development of hemorrhoid is favored by

- constipation
- prolonged standing
- excessive straining at stool
- portal hyper tension

PATHOPHYSIOLOGY

The most commonly accepted hypothesis is sliding of the anal canal lining when the supporting tissues of the anal cushions become non-functional and the anal cushions bulge downwards.The sites of the three major anal cushions are: right anterior, right posterior and left lateral. Histological evaluation of these anal cushions reveals a variety of changes. These include vascular dilatation, vascular thrombosis, degeneration of supportive tissues of the mucosa and rupture of the anal submucosal muscle. These changes are superimposed with inflammation.

CLINICAL EVALUATION

The commonest presenting feature is rectal bleeding. The bleeding is bright red in color in the form of spurts. It usually follows the passage of stools. As a result, the stools are covered with fresh blood. The bleeding at times, may be so severe that the patient may develop anemia which may, at times, be the presenting feature of hemorrhoidal disease in a select few patients. Constipation is a common accompaniment of this condition. Long term straining while passing stools is the commonest symptom. Patients spend a significant amount of time in an attempt to have a satisfying bowel evacuation. Pruritis ani may also be a symptom in cases of prolapsed piles.

INVESTIGATION

Per digital and proctoscopic examination is the first step in the diagnostic workup. Digital examination will help assessing a rectal growth as well as confirming the presence of fresh blood in the rectum. A proper proctoscopic examination will help in confirming the diagnosis. The grade of piles can be determined by a good proctoscopic examination. It is also a safe procedure to subject all patients suffering with hemorrhoids to undergo colonoscopic evaluation in order to rule out colorectal malignancy.

COMPLICATIONS

- Profuse haemorrhage
- Strangulation
- Thrombosis
- Ulceration
- Gangrene
- Fibrosis
- Suppuration
- Pylophlebitis

DIFFERENTIAL DIAGNOSIS

- Fissure in ano
- Ano-rectal abscess
- Perianal haematoma
- Prolapse of rectum

- Fistula in ano
- Portal hypertension
- Carcinoma of the rectum

TREATMENT

- Symptomatic
- Injection of sclerosant
- Banding
- Photocoagulation
- Hemorrhoidectamy

III.5. JOURNAL PUBLICATIONS OF HEMORRHOID

Review of Hemorrhoid

Zhifei sun and John Migaly(2016)published the Review of Hemorrhoid: Presentation and Management .Symptomatic hemorrhoid disease is one of the most prevalent ailments associated with significant impact on quality of life. Management options for hemorrhoid disease are diverse, ranging from conservative measures to a variety of office and operating-room procedures. In this review, the authors discussed the anatomy, pathophysiology, clinical presentation, and management of hemorrhoid disease. Anatomy and Pathophysiology:Hemorrhoids are clusters of vascular tissues, smooth muscles, and connective tissues that lie along the anal canal in three columns—left lateral, right anterior, and right posterior positions. Because some do not contain muscular walls, these clusters may be considered sinusoids instead of arteries or veins. Hemorrhoids are present universally in healthy individuals as cushions surrounding the anastomoses between the superior rectal artery and the superior, middle, and inferior rectal veins. Nonetheless, the term “hemorrhoid” is commonly invoked to characterize the pathologic process of symptomatic hemorrhoid disease instead of the normal anatomic structure.

Raakhi Mehra et al. (2011) study was carried out using a combination of apamarga kshara Basti and Triphalaguggulu.The results of the clinical assessment of the indigenous formulation on patient with Bleeding hemorrhoids were reported in this paper. The following disease criteria were used in this study.

1. Bleeding per anus
2. Pain
3. Constipation
4. Protrusion of pile mass
5. Mucus discharge
6. Itching around anus
7. Anemia

Varut lohsiriwa(2012) published the journal of Hemorrhoid from basic pathophysiology to clinical management,this review discussed the pathophysiology, epidemiology, risk factors, classification, clinical evaluation, and current non-operative and operative treatment of hemorrhoids. Hemorrhoids are defined as the symptomatic enlargement and distal displacement of the normal anal cushions. The most common symptom of hemorrhoids is rectal bleeding associated with bowel movement. The abnormal dilatation and distortion of the vascular channel, together with destructive changes in the supporting connective tissue within the anal cushion, is a paramount finding of hemorrhoids. It appears that the dysregulation of the vascular tone and vascular hyperplasia might play an important role in hemorrhoidal development, and could be a potential target for medical treatment. In most instances, hemorrhoids are treated conservatively, using many methods such as lifestyle modification, fiber supplement, suppository-delivered anti-inflammatory drugs, and administration of venotonic drugs. Non-operative approaches include sclerotherapy and, preferably, rubber band ligation. An operation is indicated when non-operative approaches have failed or complications have occurred. Several surgical approaches for treating hemorrhoids have been introduced including hemorrhoidectomy and stapled hemorrhoidopexy, but postoperative pain is invariable. Some of the surgical treatments potentially cause appreciable morbidity such as anal stricture and incontinence. The applications and outcomes of each treatment are thoroughly discussed.

Mahmoud sakre and Khaled saed(2014)published the journal of Recent advances in the management of hemorrhoids. They described that hemorrhoids are considered one of the most common anorectal diseases with a prevalence of 4.4% up to 36.4% of the general population, and a peak incidence between 45 and 65 years. Hemorrhoidal disease presents with a prolapsed lump, painless bleeding, discomfort,

discharge, hygiene problems, soiling, and pruritus. Sliding anal canal lining theory is the most accepted theory as a cause of hemorrhoidal disease; however, it is also associated with hyper-vascularity, and, recently, with several enzymes or mediators involved in the disintegration of the tissues supporting the anal cushions, such as matrix metalloproteinase. A comprehensive search in published English-language literature till 2013 involving hemorrhoids was performed to construct this review article, which discusses advances in the management of hemorrhoids. This includes conservative treatment (life style modification, oral medications, and topical treatment), office procedures (rubber band ligation, injection sclerotherapy, infrared and radiofrequency coagulation, bipolar diathermy and direct-current electrotherapy, cryosurgery, and laser therapy), as well as surgical procedures including diathermy hemorrhoidectomy, ligasure hemorrhoidectomy, Harmonic scalpel hemorrhoidectomy, hemorrhoidal artery ligation, stapled hemorrhoidopexy (SH), and double SH. Results, merits and demerits of the different modalities of treatment of hemorrhoids are presented, in addition to the cost of the recent innovations.

Ketan vagholkar et al. (2018),this publication revealed that Hemorrhoids, best described as piles in common language, is one of the most common conditions seen in colorectal clinics. Bleeding associated with chronic constipation are the presenting features of this condition. Hemorrhoids are best defined as “enlargement and distal displacement of the anal cushions.” The abnormal dilatation and irregular distortion of the vessels together with damage to the supporting connective tissue is seen within the hemorrhoids.A wide variety of therapeutic options have evolved over a period of time. However, no single option can be considered as the gold standard of treatment. Understanding the mechanisms of hemorrhoid development significantly helps in deciding the best therapeutic option.

III.6. RATIONALE OF THIS STUDY

Rathamoolam (Bleeding Hemorrhoid) is one of most prevalent ailments associated with significant impact on quality of life. Despite of its prevalence and low morbidity, hemorrhoid disease has a high impact on quality of life, and can be managed with Siddha medicine.From the review of literature, Rathamoolam has mentioned in Yugivaidya chinthamani stanza 650,which could be correlated with Bleeding Hemorrhoids in modern medicine based on symptoms. Siddha medicine provides the best alternative management as it act on the root cause of the disease.A herbal remedy is used to prevent as well as to treat or to promote healing& health. Therapeutic objective in Rathamoolam are Arrest bleeding from anus (styptic),Relieving constipation (laxative), Subsiding inflammation (anti inflammatory), Relieving pain around anus(analgesic),Relieving itching around anus(antimicrobial) and increasing Hb level(haemetenic).Recently, various research showed that all parts of Nelli(Phyllanthus emblica L) have the above said therapeutic action.Nelli Kudineer(Root,Bark,Leaf ,Fruit)is mentioned in Gunapadam Mooligai C.S.Murugesu Mudaliyar page no:621 for Rathamoolam. So, I have been selected the trial drug Nelli Kudineer(NK) for Rathamoolam(RM) as my dissertation work.

CHAPTER-IV

MATERIALS AND METHODS

STUDY DESIGN

A prospective open labelled Non randomized phase II clinical study.

STUDY PLACE

OPD &IPD of Govt.Siddha Medical College & Hospital,Palayamkottai.

SAMPLE SIZE

40 patients (20 OP&20 IP)

STUDY PERIOD

24 months from June 2017 To June 2019.

ETHICAL CLEARANCE

The trial was conducted in accordance with Ethical principles that are consistent with Good Clinical Practice guidelines and obtained prior approval before start of the trial from Institutional Ethical Committee of GSMCH, Palayamkottai. IEC number for this Trial is GSMC-IV-IEC/2017/Br-I/10,dated 29.05.2017(Annexure -I) Institutional Animal Ethical Committee(IAEC) approval obtained from K.M. College of Pharmacy, Madurai. IAEC Number for this trial is TNMGRMU/MD(S)/321611010/KMCP/29/2018, dated 01.05.2018 (Annexure -II) The trial was applied and registered in Clinical Trial Registry of India. CTRI number is CTRI/2018/03/012713, Registered on 21.03.2018(Annexure-III)

SAMPLE SELECTION

The population of study was confirmed the patients who came with the clinical features of inclusion criteria in OPD at GSMC,Palayamkottai, they were subjected to screening and documented the details using Proforma.

Inclusion Criteria

- Age:20-60 years
- Gender: Both Gender

- Patients with Rathamoolam (Bleeding Hemorrhoid) based on the disease criteria of Bleeding per anus, Pain around anus, Constipation, Protrusion of pile mass, Mucous discharge, Itchy anus and Anemia

Exclusion Criteria

- Below 20 years, Above 60 years
- Sentinel piles
- Fissure/Fistula in Ano
- Prolapse of Rectum
- Malignancy
- Rectal polyp
- Chronic Kidney, Liver and Cardiac diseases.
- Pregnant women.

Withdrawal Criteria

- Profuse bleeding
- Drug reaction
- Serious illness

TRIAL MEDICINE: NELLI KUDINEER (NK)

The siddha herbal formulation Nelli Kudineer was selected from the Gunapadam mooligai siddha text.

Ingredients of NK

Table-IV.1: Ingredients of NK

Tamil name	Botanical name	Family	Parts used	Therapeutic uses
Nelli	*Phyllanthus emblica L*	Euphorbiaceae	Root, Bark, Fruit, Leaf.	Pandu Sobai Kamalai Magotharam **Moolam** Perumpadu Megaushnam Soolai vali Moorchai Vaayu

Collection and Authentication of Nelli

The Root, Bark, Fruit and Leaf of Nelli were freshly collected from Tenkasi. It was identified and authenticated by Department of Medicinal botany (Annexure-IV) Govt. Siddha Medical college, Palayamkottai, Tirunelveli.

Purification and Preperation of Nelli

The impurities from the plants were removed, cleaned and dried in shade. An equal quantity of purified parts were taken and coarsely powdered and taken as Kudineer chooranam (KC) form. For the preparation of Kudineer, 25gm of the KC was boiled with 500 ml of water till reduced to 100ml of Kudineer(Chidambatathanu Pillai, Siddha system of Pharmacopoeia Pg no:34).This chooranam is stored in air tight clean container and issued each packets to patients. Each packet is contained 50 gm of the Kudineer chooranam. For OP cases one packet was given for 7 days and advised for periodical assessment once in seven days for one month. For IP cases, the prepared Kudineer is issued directly by me.

Dose: Kudineer 100ml, OD(morning),Before food.

Duration: 30 days

Figure- IV.1: Preperation of NK

LEAF

ROOT

FRUIT

BARK

KUDINEER CHOORANAM

KUDINEER

Panchabootha aspect of NK

Table IV.2: Panchabootha aspect of NK

Taste	**Panchabootham**	**Potency**	**Mukkutram**	**Function**
Sour	Mann+Theyu	Hot	V normalized	Proper digestion, Proper functioning of Jadarakkini, Nourishes blood vessel, Easy defaecation
Astringent	Mann+Vayu	Cold	P normalized	Constricting effect, heal ulcers, Removes PK
Sweet	Mann+Neer	Cold	V normalized Normalized theVP	Activate 5 sense organs

Vatham is normalized by Sweet,Sour,Salt.**Pitham** is normalized by Sweet,Astringent,Bitter.**Cold potency** taste which have no predominant Theyu bootha,Tastes are Astringent,Sweet,Bitter.Removes Ratham and Pitham,Increases life span, Give pleasure to mind. **Earth(Mann)** is predominant bootham in Nelli Kudineer.It evacuate the thodam within the Intestine by defaecation.It has all the qualities of other boothams.

Basic method used by Siddhars for the preparation of Siddha medicines are

1. Ekamooligai prayokam
2. Maarana prayokam
3. Dravaka prayokam
4. Cheyaneer prayokam
5. Muppuchunna prayokam

Siddha herbal preparation Nelli Kudineer is prepared based on the **Ekamooligai prayokam**, since it contains only herbal products. Here selecting the single drug or combination of drugs on the basis of boothas that is present in the drug to normalize the affected thosham.

PRECLINICAL ANALYSIS OF NK

Following preclinical studies were carried out and cross checked before starting the treatment.

Biochemical Analysis

It had done in Dept.of Biochemistry, GSMCH,Palayamkottai

Phytochemical Analysis

Qualitative phytochemical analysis was done in Biogenix lab Trivandrum. Phytochemical screening for Alkaloids, Flavanoids, Saponins, Phenol, Steroids, Glycosides, Tannins and Terpenoids were studied. The tests are used for the analysis of phytochemicals as described by Harborne and Onwukaeme were carried on Alcoholic extract of NK.

Antimicrobial assay

Antimicrobial activity by Agar-well diffusion method is used and done in Biogenix lab Trivandrum. Materials required for this study were Muller Hinton agar medium (1L), Nutrient broth (1L), Streptomycin (10mg/ml), Culture of test organisms (E.coli, Staphylococcus aureus) and growth of culture adjusted according to McFarland Standard 0.5%.

Pharmacological studies

Following pharmacological activity studies were done in K.M. College of Pharmacy, Madurai Tamilnadu.

Pharmacological Action	**Method Used**
Styptic	Blood Cloting Profile
Laxative	Measuring Faeces output
Analgesic	Acetic Acid - Induced Writhing response
Anti inflammatory	Carrageenan induced Paw edema, Pleurisy
Haemetenic	Phenyl hydrazine induced Anaemia

Toxicity study

Acute toxicity and chronic toxicity of NK is carried out as per OECD-423 guidelines. In the acute toxicity study, Female wistar albino rats were administered 60,300,2000mg for 14 days. Chronic toxicity study was carried out for 90 days. Toxicity studies were done in K.M.College of Pharmacy, Madurai Tamilnadu.

ASSESSMENT

Clinical Assessment

Raakhi Mehra et.al.(2011) disease criteria is used in this study. Grade is given accordingly to intensity and frequency of the criteria.

- Bleeding per anus
- Pain around anus
- Constipation
- Protrusion of Pile mass
- Mucous discharge
- Itchy anus
- Anemia

Siddha Assessment

- Poriyaal arithal
- Pulanal arithal
- Vinathal
- Uyir thaathukkal
- Udal thaathukkal
- Envakai thervukal
- Nilam,Kaalam,Theki

Investigations

- Routine blood examination TC, DC, ESR, Hb, Blood sugar, S.Cholesterol
- Routine urine examination: Albumin, Sugar, Deposits
- Stool examination: Ova,cyst,occult blood
- Digital Rectal Examination,
- Proctoscopy.

STUDY ENROLMENT AND ASSESSMENT

Rathamoolam patients reporting in the OPD are selected based on the inclusion criteria. The patients who are enrolled informed about the study of Trial drug, possible outcomes and the objectives of the study in their language and terms understandable to them and the informed consent is obtained. Detailed history, Physical examination, clinical assessment and Investigations were done as per the Proforma (Annexure-V).

TRIAL MONITORING AND TREATMENT.

The Guide and Supervisor monitored the progress of the trial. The Head of the Department monitored the data entries. On the first day NK chooranam packets was given to enrolled OP patients and asked to have regular follow up once in seven days for one Month. Nelli Kudineer was given to IP patients directly. The clinical assessment and Investigations were done before and after treatment and recorded in the prescribed Proforma. All the patients are instructed to follow the compatible diet and activities and Yoga and Meditation.

STATISTICAL ANALYSIS

The collected data's are presented in the form of percentage and figures. And analyzed using the SPSS. Data was expressed as Mean and Standard deviation. The significance of the difference between the mean of the baseline and final examinations was tested using the Paired "t" test. A probability value (P-value) of <0.05 was considered to be statically significant.

CHAPTER-V

RESULTS AND OBSERVATIONS

V.I. PRECLINICAL STUDY OF NELLI KUDINEER

Biochemical Analysis

5 gms of the drug was weighed accurately and placed in a 250 ml clean beaker then 50 ml of distilled water is added and dissolved well. Then it is boiled well for about 10 minutes. It is cooled and filtered in a 100ml volumetric flask and then it is made to 100 ml with distilled water. This fluid is taken for analysis.

Table -V.1.1: Result of Qualitative biochemical analysis

Sl No.	EXPERIMENT	OBSERVATION	INFERENCE
1.	Test for Calcium	White precipitate formed	Calcium present
2.	Test for Sulphate	White precipitate formed	Sulphate present
3.	Test for Chloride	White precipitate formed	Chloride present
4.	Test for Carbonate	No brisk effervessence is formed	Carbonate absent
5.	Test for Starch	No blue colour is formed	Starch absent
6.	Test for Ferric iron	No blue colour is formed	Ferric Iron absent
7.	Test for Ferrous Iron	Blood red colour is formed	Ferrous Iron present
8.	Test for Phosphate	No yellow precipitate is formed	Phosphate absent
9.	Test for Albumin	No yellow precipitate is fprmed	Albumin absent
10.	Tesst for Tannic acid	Blueblack precipitate is formed	Tannic acid present
11.	Test for Unsaturation	It gets decolourised	Unsaturated compound present
12.	Test for Reducing sugar	No colour change occur	Reducing sugar absent
13.	Test for Amino acid	Violet colour is formed	Aminoacid present
14.	Test for Zinc	No white precipitate is formed	Zinc absent

From Table-V.1.1, Analysis was noted that the *presence of calcium, sulphate, Chloride, ferrous iron, tannicacid, unsaturated compound, amino acid* and showed the absence of carbonate, starch, ferric iron, phosphate, albumin, reducing sugar, zinc.

Phytochemical Analysis

Table-V.1.2: Result of Qualitative Phytochemical analysis of NK

Phytochemicals	**Observation**	**Inference**
1.Alkaloids	An orange red precipitate produced.	Presence of alkaloids
2.Flavanoids	No characteristic change.	Absence of flavanoids
3.Phenols	A blue or green color was formed.	Presence of Phenols
4.Glycosides	A Yellow color was formed.	Presence of glycosides
5.Saponins	No characteristic change.	Absence of saponins
6.Steroids	A red color was produced in the chloroform layer.	Presence of steroids
7.Tannins	The bluish black color was disappeared in the addition of sulfuric acid, no yellow color precipitate.	Presence of tannins
8.Terpenoids	A red color was produced in the chloroform layer.	Presence of terpenoids.

The above Table –V.1.2:The qualitative Phytochemical analysis was resulted in the *presence of alkaloids, phenols, glycosides, steroids, tannins and terpenoids.*

Antimicrobial Assay

Table-V.1.3: **Gram Positive** (Organism: *Staphylococcus aureus)*

Sample	Concentration (µg/ml)	Zone of inhibition(mm)
Streptomycin	100µg	27
Nelli Kudineer	250	Nil
	500	Nil
	1000	13

Table-V.1.4: **Gram Negative** (Organism: *E.Coli)*

Sample	Concentration (µg/ml)	Zone of inhibition(mm)
Streptomycin	100µg	25
Nelli Kudineer	250	Nil
	500	10
	1000	14

According to Table- V.1.3 and V.1.4 revealed that NK extract exhibited anti microbial activity against E.Coli at concentration of 250 µg/ml was no ZIC and at 500µg/ml is 10mm zone of inhibition (ZIC) and at 1000µg/ml concentration was

14mm zone of inhibition. Antimicrobial activity of NK against *Staphylococcus aureus* at concentration of 250 & 500µg/ml was showed not sensitive to the micro organism and at 1000µg/ml zone of inhibition was 13 mm was observed from my study.

Pharmacological Activities

1. Anti-Coagulant activity NK

Table- V.1.5: Effect of NK on Blood clotting profile in wistar rats.

Groups	Bleeding time (sec)	Clotting time (sec)	Prothrombin time	Activated Thromboplastin time	Fibrinogen Time
Normal control	85.25±2.15	118.1±3.15	25.30±1.32	26.04±1.40	194.6±3.12
NK 100mg/kg	91.20±2.45*a	115.3±2.90*a	24.14±1.26*a	23.10±1.32*a	172.8±3.03*a
NK 200mg/kg	87.10±2.35*a	111.2±2.55*a	21.18±1.13*a	16.25±1.20*a	143.9±2.78*a
Standard control	82.40±1.80*a	108.2±1.94*a	18.25±0.92*a	12.55±1.02*a	117.7±2.32*a

Values are expressed as Mean± SEM.(*a Values are significantly different from Normal control at P<0.01) Table-V.1.5 resulted in analysis of the blood clotting profile of control and drug treated dose of 100 and 200mg/kg of NK was possess significant reduction in clotting time, bleeding time, prothrombin time, partial thromboplastin time and fibrogen time when compared to the control rats.

2. Laxative Action of NK

Table-V.1.6 Laxative action of NK

Groups	Drug treatment	Faeces output (gms)
I	Control Saline (10ml/kg)	3.80±0.40
II	Sodium picosulfate (5mg/kg)	12.30±1.24*
III	Nelli Kudineer100mg/kg	10.38±0.90**
IV	Nelli Kudineer200mg/kg	11.45±0.96***

Values are in Mean ± SEM; (n = 6); *P < 0.05,**P < 0.01, *** P < 0.001 Vs Control Table-V.1.6 illustrated that NK was studied for laxative action in Wistar Albino rats. The laxative action was assessed by measuring the wet faeces in all test drug administered groups. The NK showed significant (P<0.01) dose dependent laxative action as compare to normal control animals. The laxative activity produced by the NK was similar to that of the reference control sodium picosulfate. NK produced significant and dose dependant increase in faeces output of rats. Sodium picosulfate is a member of the poly phenolic group of stimulant laxatives. Following oral administration, it is converted in the colon to an active form through the action of bacterial enzymes. As a result, its effects are directed the colon, where it stimulates peristalsis and reduces water reabsorption leading to the softening of stools

3. Evaluation of Analgesic Activity of NK.

Table-V.1.7: Effects of NK on Acetic acid–induced writhing response .

Groups (N=6 in each Gp)	**Treatment**	**Number of writhing movements (Mean ± S.E)**	**Percentage %**
Group I	Distilled water	31.00 ± 2.48	
Group II	Diclofenac sodium 10mg/kg	5.72 ± 0.89*b	81.54%
Group III	100mg/kg NK	14.20 ± 1.63*b	54.19%
Group IV	200mg/kg NK	13.12 ± 1.28*b	57.67%

Values are expressed as mean ± SEM.(*b: Values are significantly different from control G2 at P<0.01) Table-V.1.7 showed that the different doses of NK had significantly noted analgesic effects in the animals. The doses of 100 & 200 mg/kg were significant & comparable with effect of Diclofenac sodium in analgesic activity .Groups of rats (n=6), were administered with 100 & 200 mg/kg of NK,10 mg /Kg Diclofenac sodium as positive control group & 1 ml distilled water as negative control group. After 30 minutes the animals were administered with i.p. injection of 0.1ml acetic acid (0.6%).Then the count of abdominal contractions of animals during 30 minutes after acetic acid injection was reported and the percentage analgesic activity (PAA) was calculated.

4. Evaluation of Carrageenan induced Anti-inflammatory Activity of NK.

Table-V.1.8: Effect of NK on Carrageenan Induced Rat Paw Edema.

Treatment group	**Dose (mg/kg, p.o.)**	**Mean increase in paw volume (ml)**	**% Decrease in paw volume**
Normal control (G1)	10ml/kg saline	0.86 ± 0.06	
Toxic control (G2)	0.1 ml, 1% carrageenan	3.38 ± 0.24*a	
Standard control (G3)	10mg/kg Indomethacin	1.26 ± 0.12*b	62.72%
Treatment control (G4)	100mg/kg NK	1.38 ± 0.16*b	59.17%
Treatment control (G5)	200mg/kg NK	1.33 ± 0.14*b	60.65%

Values are expressed as mean ± SEM. Values were compared by using analysis of variance (ANOVA) followed by Newman-Keul's multiple range tests.* (a) Values are significantly different from normal control G1 at P<0.01.* (b) Values are significantly different from Toxic control G2 at P<0.01.The above Table-V.1.8 showed the effect of NK on Carrageenan-induced Paw edema in rats. The results obtained indicate that NK had significant anti-inflammatory activity in rats. The NK reduced the edema induced by carrageenan by 59.17% and 60.65% on oral administration at 100 and 200 mg/kg as compared to the untreated control group. Indomethacin at 10 mg/kg inhibited the edema volume by 62.72%. The anti-inflammatory activity were expressed as Mean increase in paw diameter ± SD. Results were analyzed using one way ANOVA. Differences were considered as statistically significant at P < 0.05 are compared to control

Table-V.1.9:Effect of NK on Carrageenan Induced Pleurisy in Rats.

Treatment	**Dose (mg/kg, p.o.)**	**Pleural exudates (ml)**	**Leukocytes (×103 cells/ml)**
Normal control	10ml/kg saline	0.14±0.05	0.32±0.02
Toxic control	0.1 ml, 1% carrageenan	0.36±0.11*a	4.20±0.33*a
Standard control	10mg/kg Indomethacin	0.14±0.03*b	0.46±0.06*b
Treatment control	100mg/kg NK	0.21±0.08*b	0.51±0.07*b
Treatment control	200mg/kg NK	0.13±0.02*b	0.48±0.05*b

Values are expressed as mean ± SEM. Values were compared by using analysis of variance (ANOVA) followed by Newman-Keul's multiple range tests.* (a) Values are significantly different from normal control G1 at P<0.01.*(b) Values are significantly different from Toxic control G2 at P<0.01.Table-V.1.9 showed that the volume of pleural exudates in the toxic control group was 0.36±0.11 ml. Animals treated with NK(100 and 200 mg/kg, p.o.) the pleural exudates was 0.21±0.08 ml and 0.13±0.02.Treatment with Indomethacin(10 mg/kg, p.o.) produced the exudates of 0.14±0.03 ml. The leukocyte count for the control group was found to be $4.20\pm0.33\times10^3$ cells/ml. Animals treated with the trial drug and and standard produced a leukocyte migration of $0.51\pm0.07\times10^3$,$0.48\pm0.05X10^3$ and $0.46\pm0.06\times10^3$ cells/ml respectively.

5. Haematinic activity of NK in Phenyl hydrazine induced Anaemic rats

TableV.1.10: Result in Hematological Parameters of Rats

Parameters	**G1**	**G2**	**G3**	**G4**	**G5**
HB g/dl	14.40±1.40	8.28±0.94**	12.10±1.05**	12.45±1.18**	14.08±1.32**
PCV (%)	49.15±2.20	41.24±1.92	44.30±2.02**	45.18±2.08**	48.35±2.14**
RBC	4.25±0.32	4.08±0.24	4.40±0.54	4.48±0.59	4.66±0.68
MCV	76.08±2.18	92.40±2.94	86.05±2.48**	82.22±2.39**	79.35±2.28
MCH	26.15±2.45	33.84±2.90	31.55±2.85	29.28±2.68	27.46±2.58
MCHC g/dl	33.10±1.18	32.56±1.04	33.38±1.26	34.05±1.35	34.55±1.48

Values are mean±S.E.M.**P<0.01Vs Control N=6.Phenyl hydrazine is used for the induction of haemolytic anaemia and the study of its mechanism in many species including rats.Phenyl free radical produced via the 2- electron oxidation of phenyl hydrazine by oxyhemoglobin. This free radical binds with red cell and hemolyses it rapidly and converts oxyhemoglobin into methemoglobin. Thus, PHZ-induced hemolytic injury seems to be derived from oxidative alterations to red blood cell

proteins rather than to membrane lipids.The RBC,Hb,and PCV of rats administered Phenyl hydrazine decreased significantly (P <0.01) while the MCV and MCH increased giving rise to macrocytic anaemia (P<0.05).NK at oral doses of 100mg and 200mg showed increased in haemoglobin level is represented in Table-V.1.10. Significant increase in Hb(p<0.01)was observed when compared to positive control and it was comparable to standard drug used in this study. Phenyl hydrazine altered the haematological parameters by haemolysis characterized by decrease in haemoglobin concentration, total RBC and PCV on day 7.However,the haematological parameters were restored to normal range after treatment with NK at single oral doses of 100mg and 200mg for 14 days. Effective changes were observed after one week of treatment of anaemic rats with NK at oral doses of 100mg and 200mg reversed the influence of Phenyl hydrazine resulting to a significant (P<0.05) increase in RBC, Hb and PCV. The Hb, RBC and PCV reached near normal at the second week of the treatment. Also the recovery was progressive such that after 1week of continuous treatment, the Hb concentration and PCV were higher in the treated groups than in the normal control group.

Toxicity study with NK

A: Acute toxicity study with NK

Table-V.1.11: Acute toxicity study with NK

Group	Dose ($mg.kg^{-1}$)	Sign of Toxicity ($ST.NB^{-1}$)	Mortality ($D.S^{-1}$)
I	0	0/3	0/3
II	300	0/3	0/3
III	2000	0/3	0/3

ST- sign of toxicity; NB- normal behaviour; D- died; S- survive. Values are expressed as number of animals (n=3). The acute toxicity of NK was evaluated using OECD- 423 guidelines. There was no mortality or morbidity observed in Female wistar albino rats through the 15-days period following single oral administration at all selected dose levels of the NK(Table-V.1.11). The animals did not show any changes in the general appearance during the observation period. Morphological characteristics such as fur, skin, eyes and nose appeared normal. No tremors, convulsion, salivation, diarrhea, lethargy or unusual behaviors such as self mutilation, walking backward and so forth were observed. Gait and posture, reactivity to handling or sensory stimuli, grip strength was also normal.

B. Chronic toxicity study with NK

6.B.1: Effects of NK on Body weight changes in Rats.

Table-V.1.12: Effects of NK on Body weight changes in Rats.

Treatment	**Day 1**	**Day 30**	**Day 60**	**Day 90**
Control	188.15±6.8	188.45 ±6.20	197.15 ±6.35	197.7±6.58
NK:50 mg.kg^{-1}	195.30 ±6.4	194.30 ±6.30	199.25 ±6.70	199.30±6.72*
NK:100 mg.kg^{-1}	187.35 ±5.7	190.30 ±6.40	197.55 ±7.10	198.36±6.30*
NK:200 mg.kg^{-1}	196.30 ±7.2	199.15±6.50	199.90 ±7.20**	207.45±7.26**
NK:400 mg.kg^{-1}	188.65 ±6.05	193.15 ±5.60	196.60 ±6.35**	208.66±7.38**

Table-V.1.12 showed the effects of NK on body weight changes in rats. Group I animals were treated with normal saline (5 ml.kg^{-1}), group II animals with 50 mg.kg^{-1} of NK, group III animals with 100 mg.kg^{-1} of NK, group IV animals with 200 mg.kg^{-1} of NK, group V animals with 400 mg.kg^{-1}NK. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01 *P<0.05. The effect of NK was observed for their effect on the body weight changes from the study it was observed that, there was significant increase (p<0.05) in body weight in all the animals were observed.

6.B.2: Effect of NK on Kidney, Heart, Liver and Brain in rats

Table-V.1.13: The changes in internal organs with NK

Treatment	**Heart (gms)**	**Kidney (gms)**	**Liver (gms)**	**Brain (gms)**
Control	0.35 ± 0.05	0.65± 0.03	3.36± 0.05	0.68± 0.05
NK@50 mg.kg^{-1}	0.36± 0.02	0.81± 0.03	3.48± 0.03	0.72± 0.3
NK@100 mg.kg^{-1}	0.37± 0.06	0.79± 0.04	3.42±0.02	0.69± 0.2
NK@ 200 mg.kg^{-1}	0.36± 0.04	0.74± 0.02	3.38± 0.02	0.76± 0.05
NK@400 mg.kg^{-1}	0.35± 0.03	0.75± 0.03	3.41± 0.03	0.78± 0.05

Table-V.1.13 showed the effects of NK on kidney, heart, liver and brain of the rats. Where, group I animal treated with normal saline (5 $ml.kg^{-1}$), group II animals with 50 $mg.kg^{-1}$ of NK, group III animals with 100 $mg.kg^{-1}$ of NK, group IV animals with 200 $mg.kg^{-1}$ of NK, group V animals with 400 $mg.kg^{-1}$NK. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV,and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01.From the study it was clear that, significant (p<0.01) changes in the weights of various organs of the animals occurred with higher doses of the extract (400 $mg.kg^{-1}$ bwt), but macroscopic examinations did not show any changes in color of the organs of the treated animals compared with the control.

6.B.3: Effect of NK on biochemical profiles of Glucose and Lipids in rats

Table-V.1.14: Effects of NK on Biochemical parameters of Glucose and Lipids

Treatment group	Glucose ($mg.dl^{-1}$)	Cholesterol ($mg.dl^{-1}$)	Triglyceride ($mg.dl^{-1}$)	HDL ($mg.dl^{-1}$)	LDL ($mg.dl^{-1}$)
Control	97.65± 0.62	41.62± 0.56	30.25± 0.45	138.25± 0.55	84.15±1.72
NK@ 50 $mg.kg^{-1}$	95.50± 0.56	27.85± 0.25*	15.22± 0.23*	178.28± 0.65*	72.59±1.28
NK@ 100 $mg.kg^{-1}$	92.45± 0.47	29.74± 0.26*	17.42± 0.28*	168.18±0.78*	69.84±1.10
NK@ 200 $mg.kg^{-1}$	93.25± 0.55**	35.18± 0.30	19.84± 0.38*	187.30± 0.84*	48.60±1.30
NK@ 400 $mg.kg^{-1}$	87.25± 0.45**	34.78± 0.28	20.28± 0.34*	185.2± 0.85*	46.50±0.84

Table-V.1.14 revealed the effect of NK on Glucose and Lipids level. Group I animals treated with normal saline (5 $ml.kg^{-1}$), group II animals with 50 $mg.kg^{-1}$ of NK, group III animals with 100 $mg.kg^{-1}$ of NK, group IV animals with 200 $mg.kg^{-1}$ of NK, group V animals with 400 $mg.kg^{-1}$NK. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01 *P<0.05. The Significant decrease (p<0.05) in the plasma total cholesterol (TC), triglyceride (TG) and LDL-cholesterol levels were observed. But a significant increase (p<0.05) in HDL-cholesterol levels were observed in all the treated animals compared with the control animals

6.B.4: Effects of NK on Biochemical Parameters of Liver

Table-V.1.15:The effects of NK on biochemical parameters of Liver

Treatment group	AST ($IU.l^{-1}$)	ALT ($IU.l^{-1}$)	ALP ($IU.l^{-1}$)	TP ($g.l^{-1}$)	ALBUMIN ($g.l^{-1}$)
Control	320.5±12.40	68.5± 3.18	253.58± 8.80	69.85± 3.32	39.15±2.35
NK@50 $mg.kg^{-1}$	309.0±9.50**	66.5± 2.20**	266.10± 2.75**	70.30± 2.32	36.30±2.65
NK@ 100 $mg.kg^{-1}$	310.3±7.20**	64.1± 3.15**	260.18± 6.70**	80.15± 2.82	38.30±3.05
NK@ 200 $mg.kg^{-1}$	305.4±7.95	59.4± 2.90	265.00± 5.20	69.25± 3.32	40.20±2.75
NK@ 400 $mg.kg^{-1}$	315.2± 8.20	61.3± 3.52	269.40± 4.40	74.05± 2.58	39.48±2.70

A study on the effects (Table-V.1.15) of NK on biochemical parameters of liver such as AST, ALT, ALP, TP and Albumin rats was tested. where, group I animals were treated with normal saline ($5ml.kg^{-1}$), group II animals with 50 $mg.kg^{-1}$ of NK, group III animals with 100 $mg.kg^{-1}$of NK, group IV animals with 200 $mg.kg^{-1}$ of NK, and group V animals with 400 $mg.kg^{-1}$NK.The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01 *P<0.05.AST, ALT and ALP levels were also normal in the NK treated animals. From the results of biochemical study there was no evidence of severe toxicity associated with the administration of higher concentration of NK.

6.B.5. Effect of NK on Hematological parameters Hb,RBC,WBC,Calcium in rats

Table-V.1.16:Effects of NK on Hematological parameters

Treatment group	Hemoglobin ($mg.dl^{-1}$)	RBC ($10^6/mm^3$)	WBC ($10^6/mm^3$)	Calcium ($mg.dl^{-1}$)
Control	12.3± 0.25	9.15± 0.02	11.45± 0.05	9.45 ±0.02
NK@ 50 $mg.kg^{-1}$	13.5± 0.26*	9.50± 0.04*	9.55± 0.01*	9.21 ±0.02
NK@ 100 $mg.kg^{-1}$	13.3± 0.15*	9.55± 0.02*	8.35± 0.32*	9.27 ±0.20
NK@ 200 $mg.kg^{-1}$	11.7± 0.20*	8.33± 0.12*	11.45± 0.03*	9.61 ±0.13
NK@ 400 $mg.kg^{-1}$	12.5± 0.35*	8.51± 0.45*	10.55±0.13*	9.75 ±0.02

The effects of NK were observed (Table-V.1.16) for its effect on hematological parameters on the experimental rats. From the study it was evident that, a significant increase ($p<0.01$) were observed in the hemoglobin contents and RBC count in the group treated with NK 200 $mg.kg^{-1}$ body weight and a significant decrease of the parameters occurred in the group treated with 400 $mg.kg^{-1}$ bw compared with the control. There was no significant change in the calcium level in all the treated animals compared to the control. Where, group I animal treated with normal saline ($5\ ml.kg^{1}$), group II animals with 50 $mg.kg^{-1}$ of NK, group III animals with 100 $mg.kg^{-1}$ of NK, group IV animals with 200 $mg.kg^{-1}$ of NK, and group V

animals with 400 mg.kg^{-1}NK. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV and V. The statistical analysis was carried out using one way ANOVA method, where *P<0.05.

V.2. CLINICAL STUDY

This study was hospital based Prospective open labelled phase II Non-randomized clinical study of Nelli Kudineer for Rathamoolam (Bleeding Hemorrhoids). This study was covered 40 Rathamoolam patients, they were came from different parts of Tirunelveli. The Trial drug NK was given to selected patients and evaluated its therapeutic efficacy clinically for Rathamoolam.

The results were observed with respect to the following criteria by clinical study on 20 outpatients and 20 inpatients of both sexes. The criteria were,

1. Distribution of Gender
2. Distribution of Age
3. Distribution of Religion
4. Distribution of Educational status
5. Distribution of Occupation
6. Distribution of Socio economic status
7. Distribution of Marital status
8. Distribution of Family History
9. Distribution of Dietary habits
10. Distribution of Addiction
11. Distribution of Sleep
12. Distribution of History of previous treatment
13. Distribution of Nilam
14. Distribution of Kaalam
15. Distribution of Thegi
16. Distribution of Gunam

17. Distribution of Kanmenthiriyam

18. Distribution of Aasayangal

19. Distribution of Kosangal

20. Distribution of Uyirthathukkal

21. Distribution of Udalthathukkal

22. Distribution of Naadi

23. Distribution of Envakaithervu

24. Distribution of Neikkuri

25. Distribution of Clinical presentation

26. Distribution of Disease criteria

27. Distribution of Duration of illness

28. Distribution of Aggravating factors

29. Distribution of Degree of Hemorrhoids

30. Distribution of Change of Symptoms

31. Distribution of Hb level

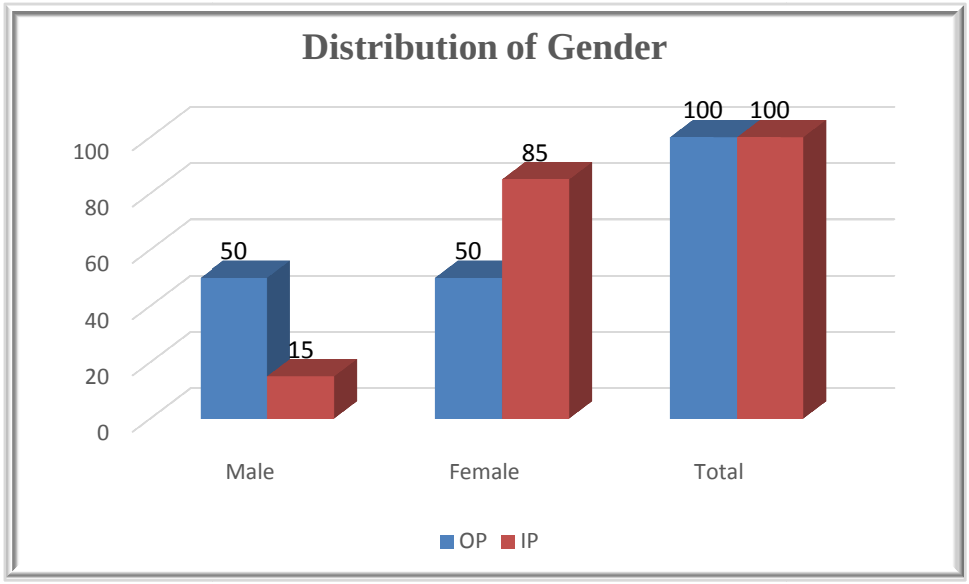
32. Distribution of Gradation of Results

V.2.1.Distribution of Gender

Table-V.2.1: Distribution of gender

Gender	OP		IP	
	No of cases	Percentage	No of cases	Percentage
Male	10	50	03	15
Female	10	50	17	85
Total	20	100	20	100

Figure-V.2.1: Distribution of Gender



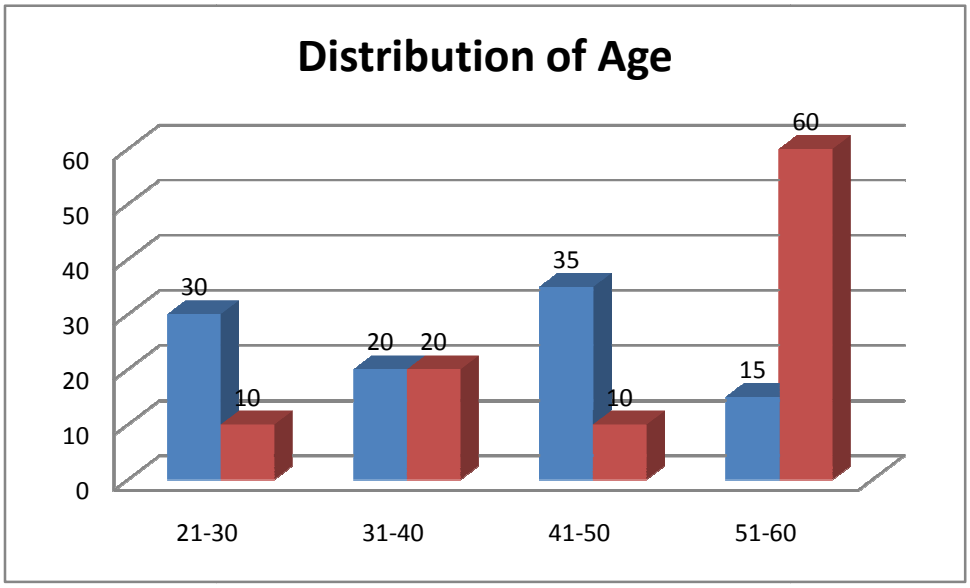
Above Table-V.2.1&Figure-V.2.1 shows among 20 OP, 50% were Female and 50% were Male, among 20 IP 85% were Female and 15% were Male.

V.2.2: Distribution of Age

Table-V.2.2: Distribution of Age and its percentage

Age group(years)	OP		IP	
	Number of cases	%	Number of cases	%
21-30	6	30	2	10
31-40	4	20	4	20
41-50	7	35	2	10
51-60	3	15	12	60
Total	20	100	20	100

Figure-V.2.2.Distribution of Age



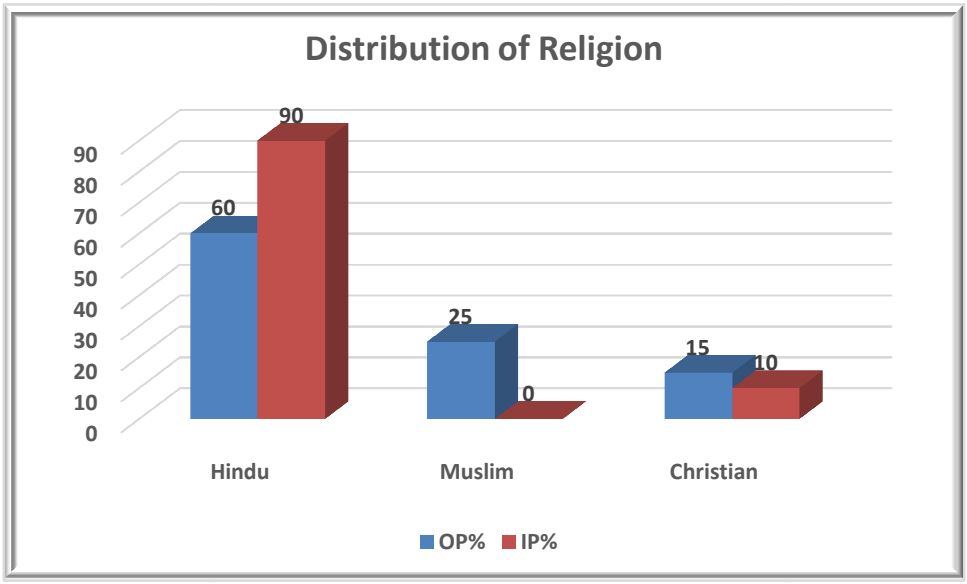
Above Table-V.2.2 and Figure-V.2.2 Illustrated that among OP most of the cases were between the age group of 41-50 i.e.35%. The most of the IP cases were between the age group of 51-60 i.e.60%.

V.2.3: Distribution of Religion

Table-V.2.3: Distribution of Religion

Religion	OP		IP	
	No of cases	%	No of cases	%
Hindu	12	60	18	90
Muslim	5	25	0	0
Christian	3	15	2	10
Total	20	100	20	100

Figure-V.2.3: Distribution of Religion



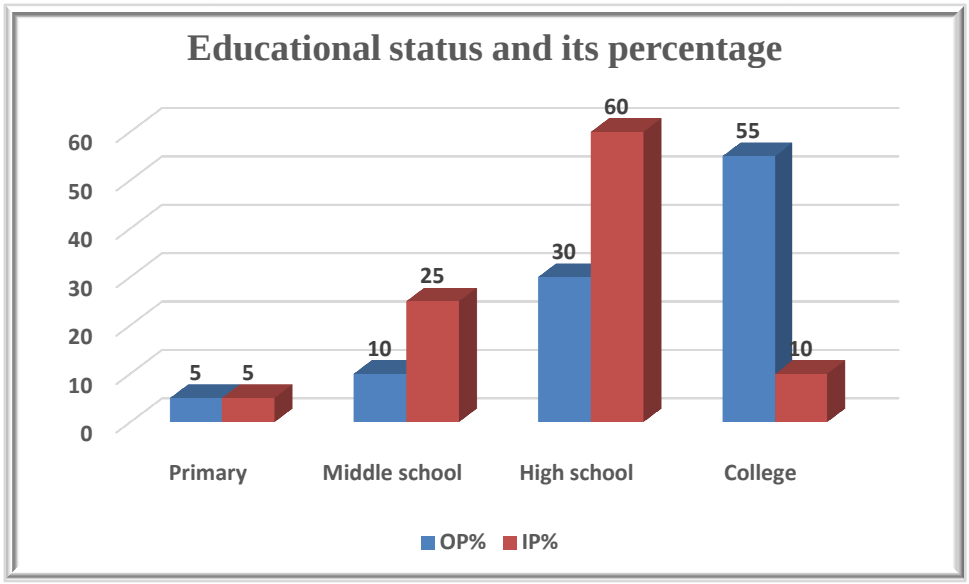
From the Table-V.2.3 and Figure-V.2.3 revealed that among OP population 60% were Hindus, 25% were muslims and 15% were Christians. Among IP populations 90% were Hindus and 10% were Christians.

V.2.4: Distribution of Educational status

Table-V.2.4: Educational status and its percentage

Educational status	**OP**		**IP**	
	No of cases	**%**	**No of cases**	**%**
Primary	1	5	1	5
Middle school	2	10	5	25
High school	6	30	12	60
College	11	55	2	10
Total	**20**	**100**	**20**	**100**

Figure-V.2.4: Distribution of Educational status



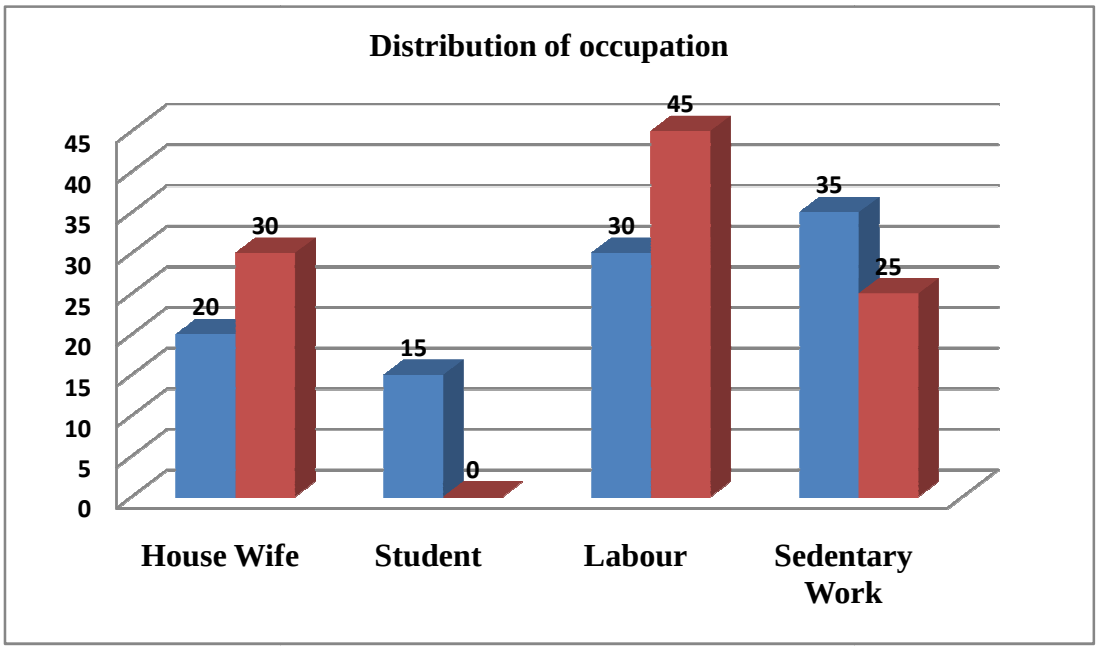
Above Table-V.2.4 and Figure-V.2.4 showed that 55% of OP cases had the college level education. 60% of IP cases had the high school level education.

V.2.5: Distribution of Occupation

Table-V.2.5: Distribution of Occupation and its percentage

Occupation	OP		IP	
	No of cases	%	No of cases	%
House Wife	4	20	6	30
Student	3	15	0	0
Labour	6	30	9	45
Sedentary Work	7	35	5	25
Total	20	100	20	100

Figure-V.2.5:Distribution of Occupation



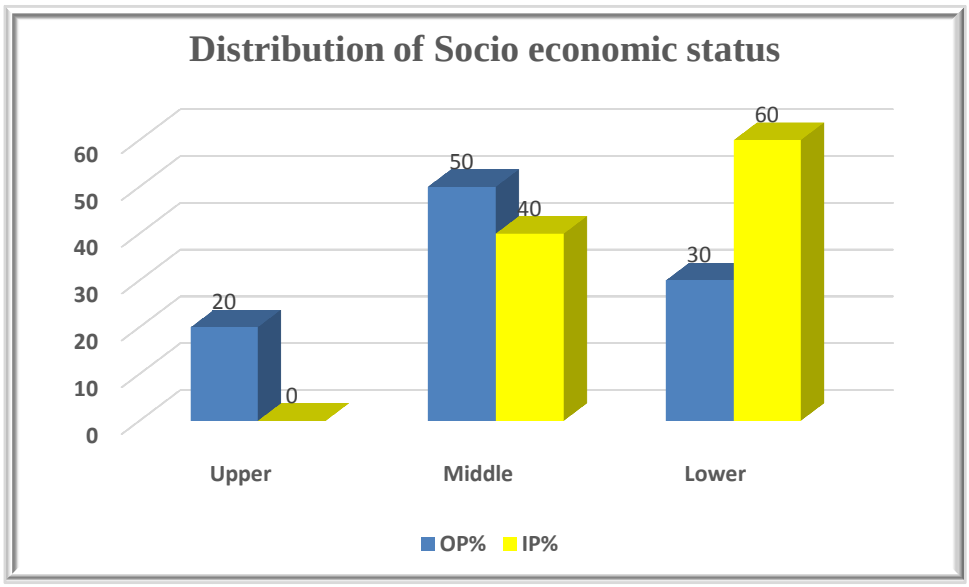
Above Table-V.2.5 and Figure-V.2.5. revealed that high prevalance in sedentary workers (35%) and labours (30%) among OP. Among IP high prevalence in labour (45%) and sedentary work (25%).

V.2.6: Distribution of Socio economic status

Table-V.2.6: Distribution of Socio economic status and its Percentage

Socio economic status	OP		IP	
	No of cases	%	No of cases	%
Upper	4	20	0	0
Middle	10	50	8	40
Lower	6	30	12	60
Total	20	100	20	100

Figure-V.2.6: Distribution of Socio economic status



Above Table -V.2.6and Figure-V.2.6showed that High prevalence from middle economic family in OP population (50%) and from Lower economic status in IP population(60%).

V.2.7: Distribution of Marital status

Table-V.2.7: Distribution of Marital status and its Percentage

Marital status	OP		IP	
	No of cases	%	No of cases	%
Married	13	65	19	95
Unmarried	7	35	1	5
Total	20	100	20	100

Figure-V.2.7: Distribution of Marital status

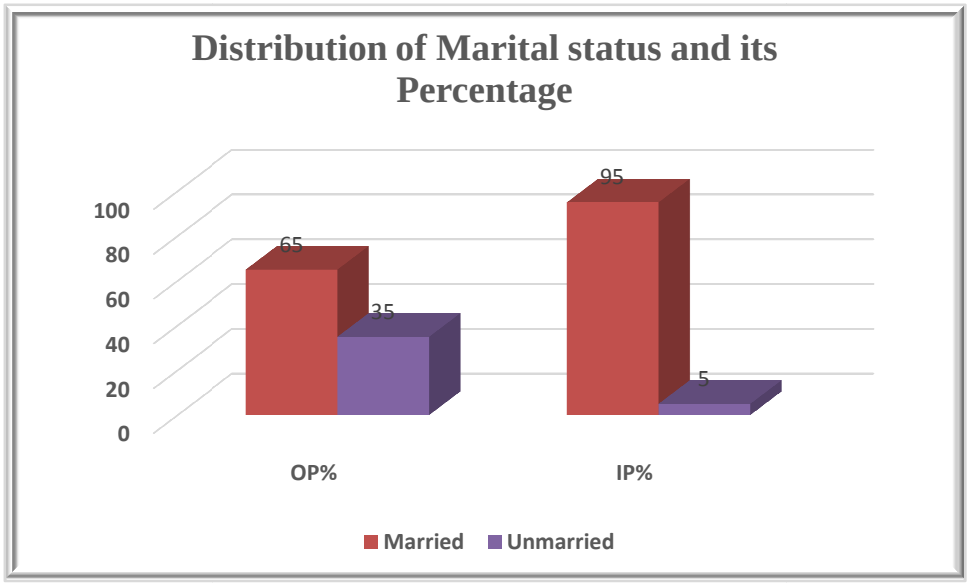


Table -V.2.7and Figure- V.2.7showed that 65% OP population were married and 95% were married in IP population.

V.2.8: Distribution of Family history of Hemorrhoids

Table-V.2.8: Distribution of Family history of Hemorrhoids and its Percentage

Family history of Hemorrhoids	OP		IP	
	No of cases	%	No of cases	%
Yes	8	40	6	30
No	12	60	14	70
Total	20	100	20	100

Figure-V.2.8: Distribution of Family history of Hemorrhoids

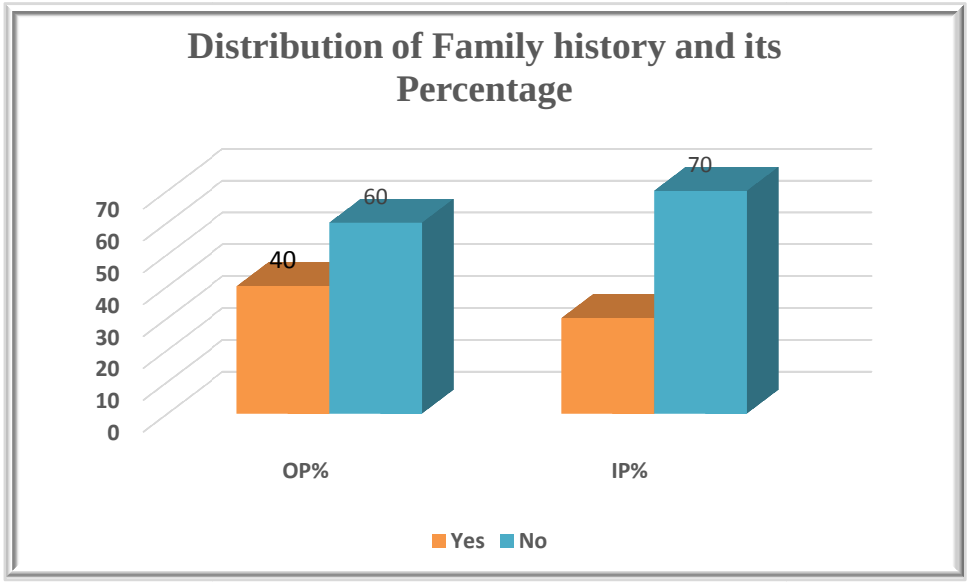


Table-V.2.8 and Figure-V.2.8 showed that 40% OP population had family history of Hemorrhoids and 30% of IP population had family history of Hemorrhoids.

V.2.9: Distribution of Dietary habits

Table-V.2.9: Distribution of Dietary habits

Dietary habits	OP		IP	
	No of cases	%	No of cases	%
Vegetarian	5	25	2	10
Mixed diet	15	75	18	90
Timely	4	20	3	15
Untimely food	16	80	17	85

Figure-V.2.9: Distribution of Dietary habits

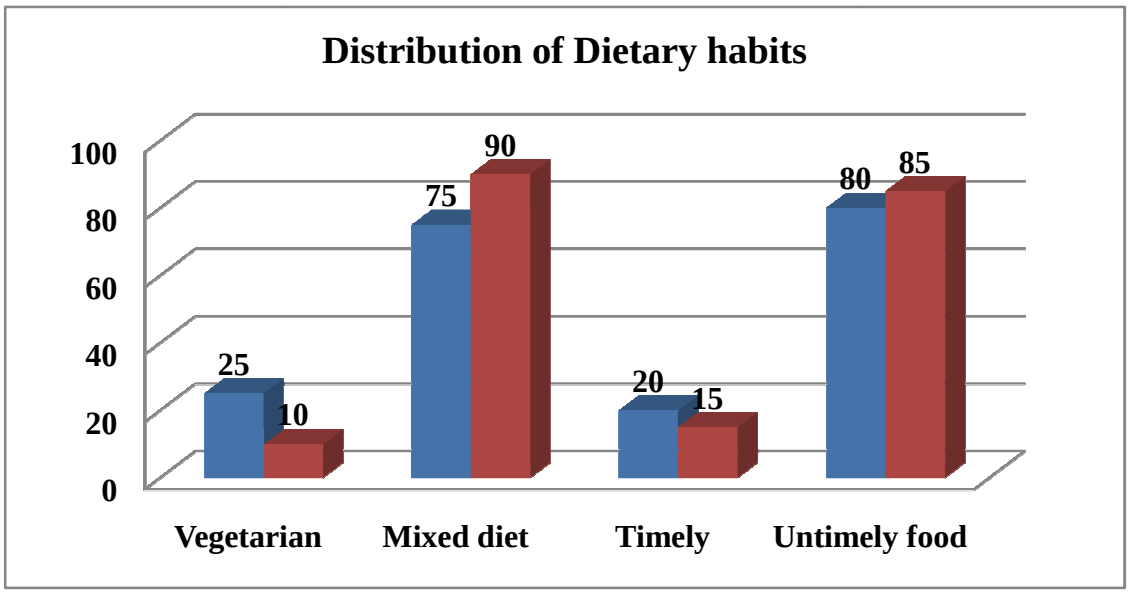


Table-V.2.9 and Figure-V.2.9 revealed that high prevalence of dietary habits include Mixed diet(75%),Untimely food(80%) among OP cases. In IP cases, high prevalence of dietary habits include Mixed diet(90%),Untimely food(85%).

V.2.10: Distribution of Addiction

Table-V.2.10: Distribution of Addiction

Addiction	OP		IP	
	No of cases	%	No of cases	%
Smoking	3	15	2	10
Alcohol	2	10	1	5
Tobacco chewing	3	15	2	10
Coffee	8	40	9	45
Tea	12	60	11	55

Figure-V.2.10: Distribution of Addiction

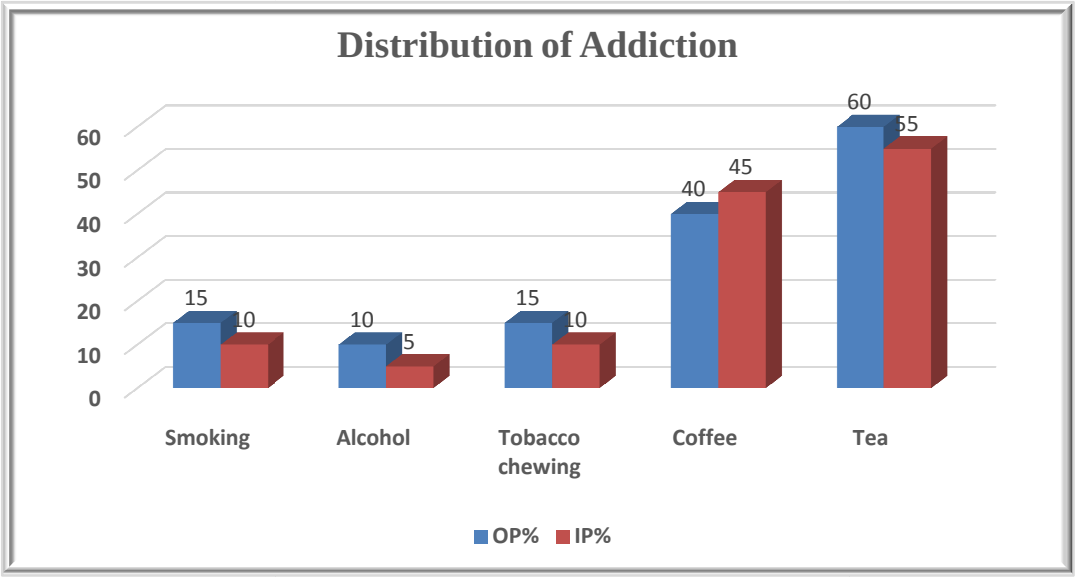


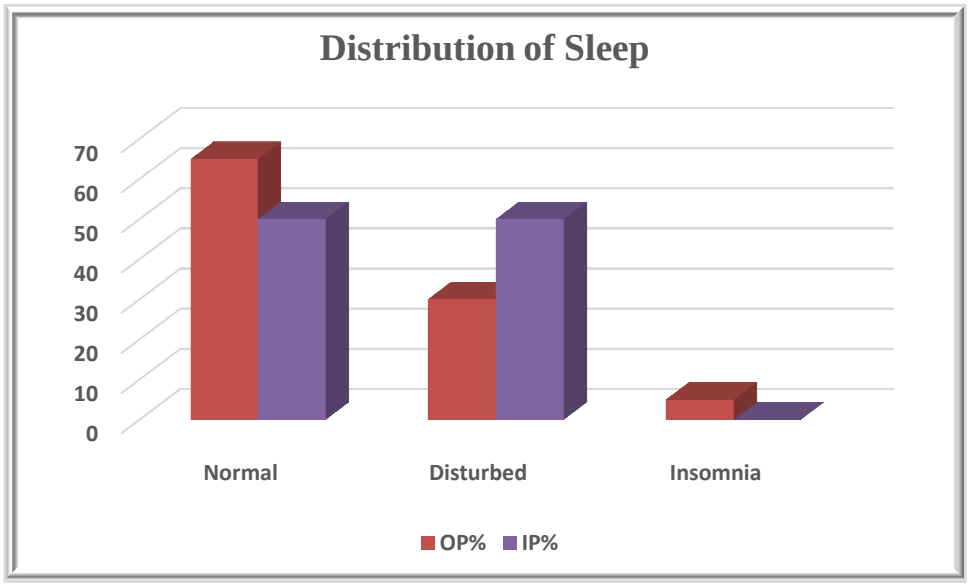
Table-V.2.10 and Figure-V.2.10 revealed that 60% OP cases have tea addiction and 40% cases have coffee addiction. Among IP population, 55% have tea addiction and 45% have coffee addiction.

V.2.11: Distribution of Sleep

Table-V.2.11: Distribution of sleep

Sleep	OP		IP	
	No of cases	%	No of cases	%
Normal	13	65	10	50
Disturbed	6	30	10	50
Insomnia	1	5	0	0
Total	20	100	20	100

Figure-V.2.11: Distribution of Sleep



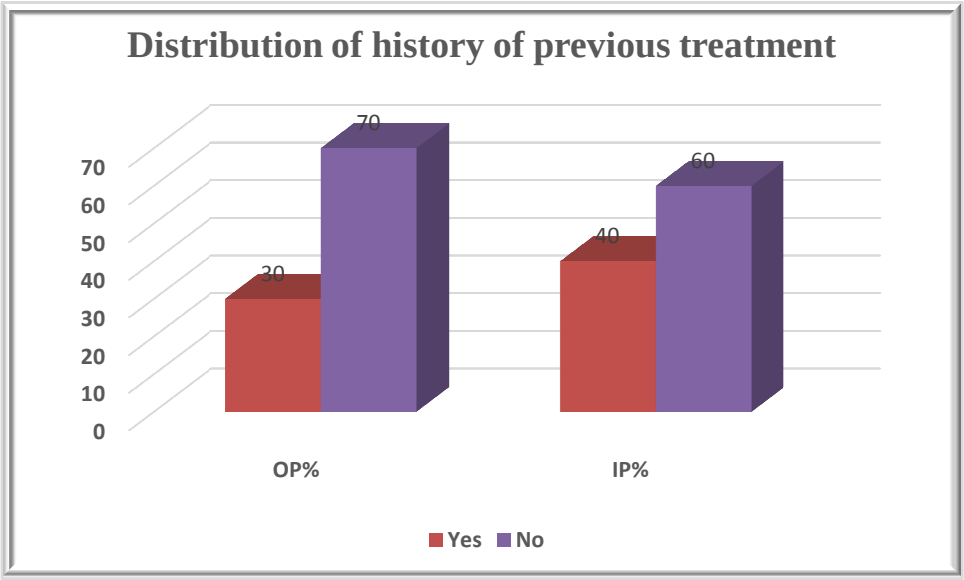
Above Table-V.2.11and Figure-V.2.11 showed that sleep was disturbed in 30% of OP cases and 50% of IP cases.

V.2.12.Distribution of History of previous treatment

Table-V.2.12: Distribution of History of previous treatment

Previous treatment	OP		IP	
	No of cases	%	No of cases	%
Yes	6	30	8	40
No	14	70	12	60

Figure-V.2.12: Distribution of history of previous treatment



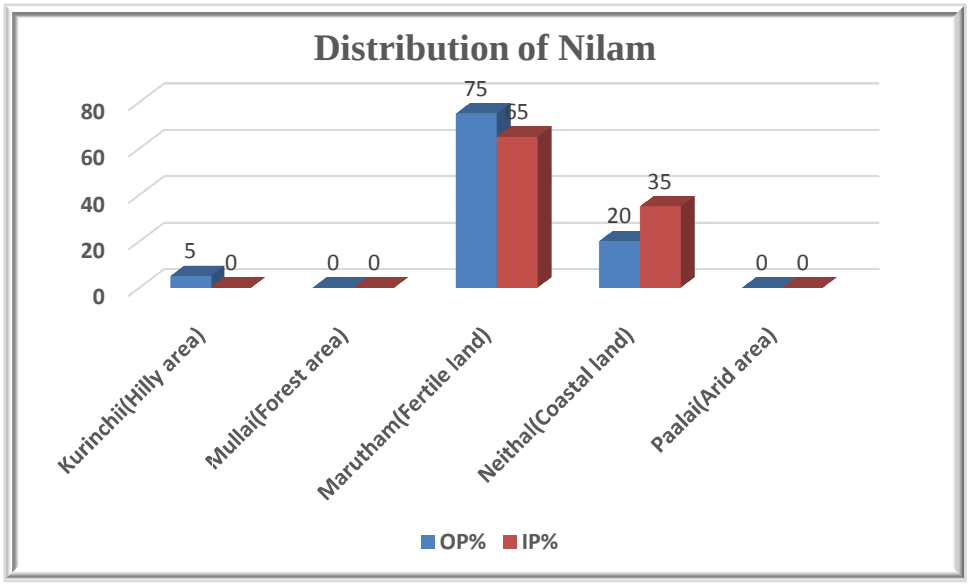
Above Table-V.2.12 and Figure-V.2.12 revealed that, In OP population 30% were had history of previous treatment and among IP 40% were had history of previous treatment.

V.2.13: Distribution of Nilam

Table-V.2.13: Distribution of Nilam

Nilam	OP		IP	
	No of cases	%	No of cases	%
Kurinchii(Hilly area)	01	5	0	0
Mullai(Forest area)	0	0	0	0
Marutham(Fertile land)	15	75	13	65
Neithal(Coastal land)	04	20	07	35
Paalai(Arid area)	0	0	0	0
Total	20	100	20	100

Figure: V.2.13 Distribution of Nilam



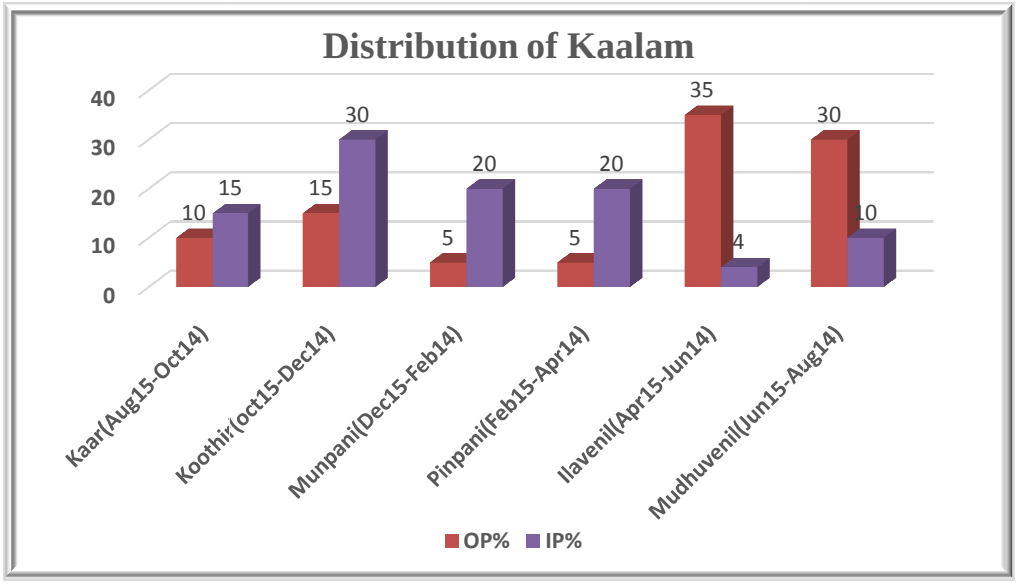
Above Table-V.2.13 and Figure-V.2.13revealed that, In OP population 75% were from Marutha nilam and 20% were from Neithal, In IP population 65% were from Marutha nilam and 35% were from Neithal.

V.2.14: Distribution of Kaalam

Table-V.2.14: Distribution of Kaalam

Kaalam	OP		IP	
	No of cases	%	No of cases	%
Kaar(Aug15-Oct14)	2	10	3	15
Koothir(oct15-Dec14)	3	15	6	30
Munpani(Dec15-Feb14)	1	5	4	20
Pinpani(Feb15-Apr14)	1	5	4	20
Ilavenil(Apr15-Jun14)	7	35	1	4
Mudhuvenil(Jun15-Aug14)	6	30	2	10
Total	20	100	20	100

Figure-V.2.14: Distribution of Kaalam



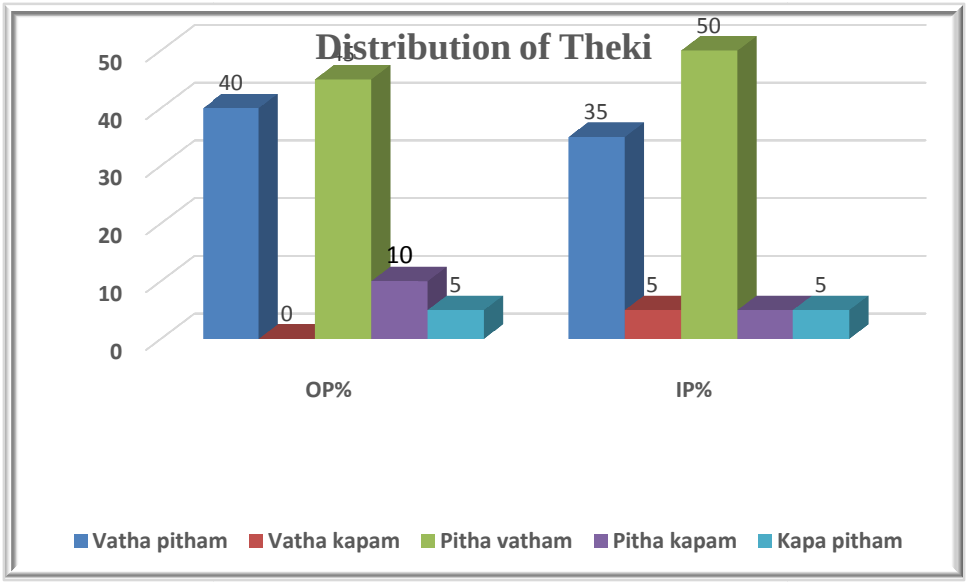
Above Table -V.2.14 and Figure- V.2.14showed that Among OP population,35% were affected in Ilavenil and Muthuvenil(30%) kaalam, Among IP population, 30% cases affected in koothir,20% affected in Munpani and Pinpani kaalam

V.2.15: Distribution of Theki

Table-V.2.15: Distribution of Theki

Theki	OP		IP	
	No of cases	%	No of cases	%
Vatha pitham	8	40	7	35
Vatha kapam	0	0	1	5
Pitha vatham	9	45	10	50
Pitha kapam	2	10	1	5
Kapa pitham	1	5	1	5
Total	20	100	20	100

Figure-V.2.15: Distribution of Theki



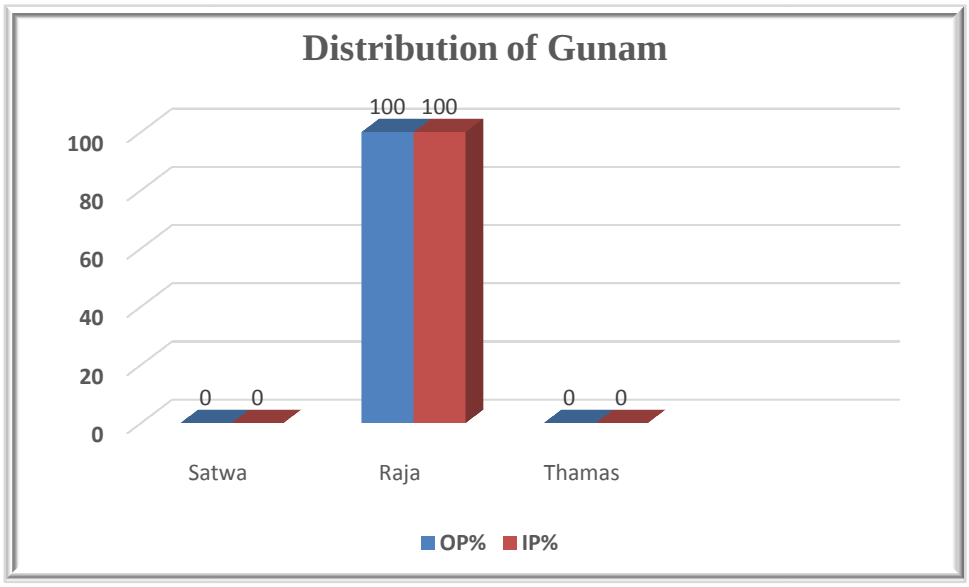
AboveTable-V.2.15 and Figure-V.2.15illustrated that 45 %patients were Pitha Vatha theki and 40% patients were Vatha Pitha theki among OP cases.50% cases were Pitha vatha theki and 35% cases were Vatha Pitha Theki among IP.

V.2.16: Distribution of Gunam

Table-V.2.16: Distribution of Gunam

Gunam	OP		IP	
	No of cases	%	No of cases	%
Satwa	-	-	-	-
Rajas	20	100	20	100
Thamas	-	-	-	-
Total	20	100	20	100

Figure-V.2.16: Distribution of Gunam



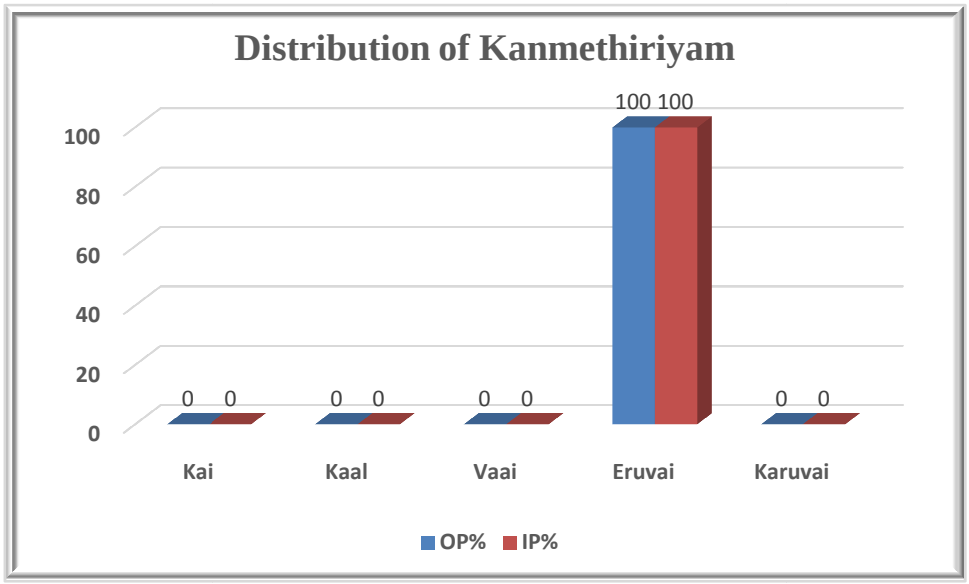
Above Table -V.2.17 and Figure- V.2.17 showed that 100% of the affected patients in IP & OP having Rajogunam.

V.2.17: Distribution of Kanmethiriyam

Table-V.2.17: Distribution of Kanmethiriyam

Kanmenthiriyam	OP		IP	
	No of cases	%	No of cases	%
Kai	-	-	-	-
Kaal	-	-	-	-
Vaai	-	-	-	-
Eruvai	20	100	20	100
Karuvai	-	-	-	-

Figure-V.2.17:Distribution of Kanmenthiriyam



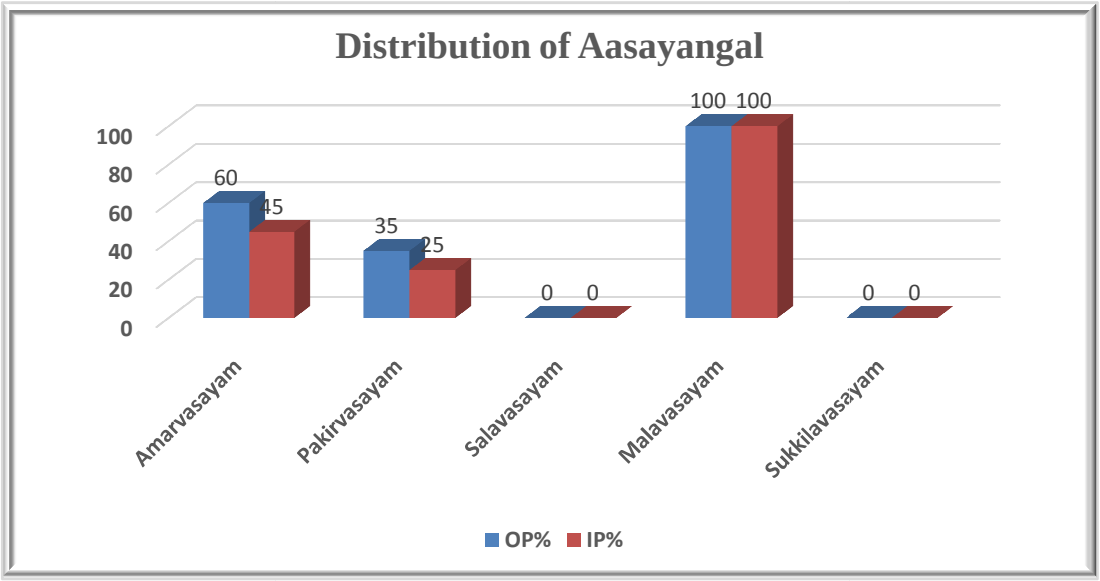
Above Table -V.2.17 and Figure- V.2.17 showed that among 20 OP, eruvai was affected in 100% cases,, among 20 IP eruvai was affected in 100% cases.

V.2.18: Distribution of Aasayangal

Table-V.2.18: Distribution of Aasayangal

Aasayangal	OP		IP	
	No of cases	%	No of cases	%
Amarvasayam	12	60	9	45
Pakirvasayam	7	35	5	25
Salavasayam	0	0	0	0
Malavasayam	20	100	20	100
Sukkilavasayam	0	0	0	0

Figure -V.2.18:Distribution of Aasayangal



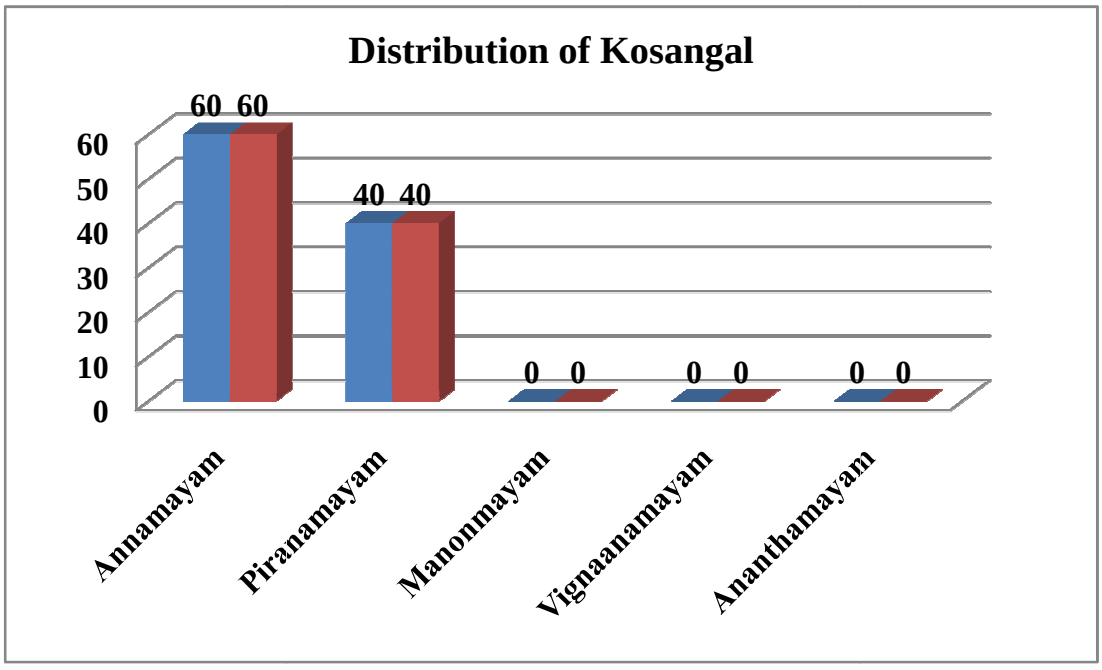
Above Table -V.2.18 and Figure- V.2.18 showed that among 20 OP, amarvasayam was affected in 60% cases, pakirvasayam was affected in 35% cases, malavasayam was affected in 100% cases, among 20 IP, amarvasayam was affected in 45% cases, pakirvasayam was affected in 25% cases, malavasayam was affected in 100% cases.

V.2.19: Distribution of Kosangal

Table-V.2.19: Distribution of Kosangal

Kosangal	OP		IP	
	No of cases	%	No of cases	%
Annamayam	12	60	12	60
Piranamayam	8	40	8	40
Manonmayam	-	-	-	-
Vignaanamayam	-	-	-	-
Ananthamayam	-	-	-	-

Figure- V.2.19: Distribution of Kosangal



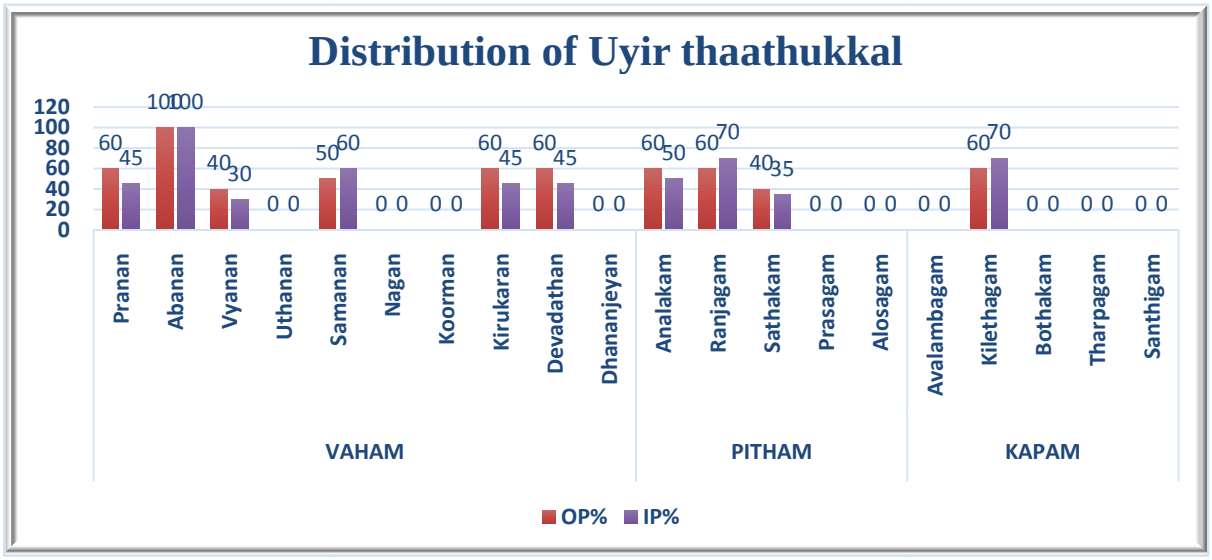
Above Table -V.2.19 and Figure- V.2.19 showed that among 20 OP, Annamayakosam was affected in 60% cases, piranamayam was affected in 40% cases, among 20 IP, Annamayakosam was affected in 60% cases, piranamayam was affected in 40% cases.

V.2.20: Distribution of Uyir thaathukkal

Table-V.2.20: Distribution of Uyir thaathukkal

Uyir thaathukkal	OP		IP	
	No of cases	%	No of cases	%
Vatham				
• Pranan	12	60	9	45
• Abanan	20	100	20	100
• Viyanan	8	40	6	30
• Uthanan	-	-	-	-
• Samanan	10	50	12	60
• Naagan	-	-	-	-
• Koorman	-	-	-	-
• Kirukiran	12	60	9	45
• Devathathan	12	60	9	45
• Dhananjeyan	-	-	-	-
Pitham				
• Analakam	12	60	10	50
• Ranjakam	12	60	4	70
• Sathakam	8	40	7	35
• Prasakam	-	-	-	-
• Aalosakam	-	-	-	-
Kapam				
• Avalampakam	-	-	-	-
• Kilethakam	12	60	14	70
• Bothakam	-	-	-	-
• Tharpakam	-	-	-	-
• Santhikam	-	-	-	-

Figure- V.2.20: Distribution of Uyir thathukkal



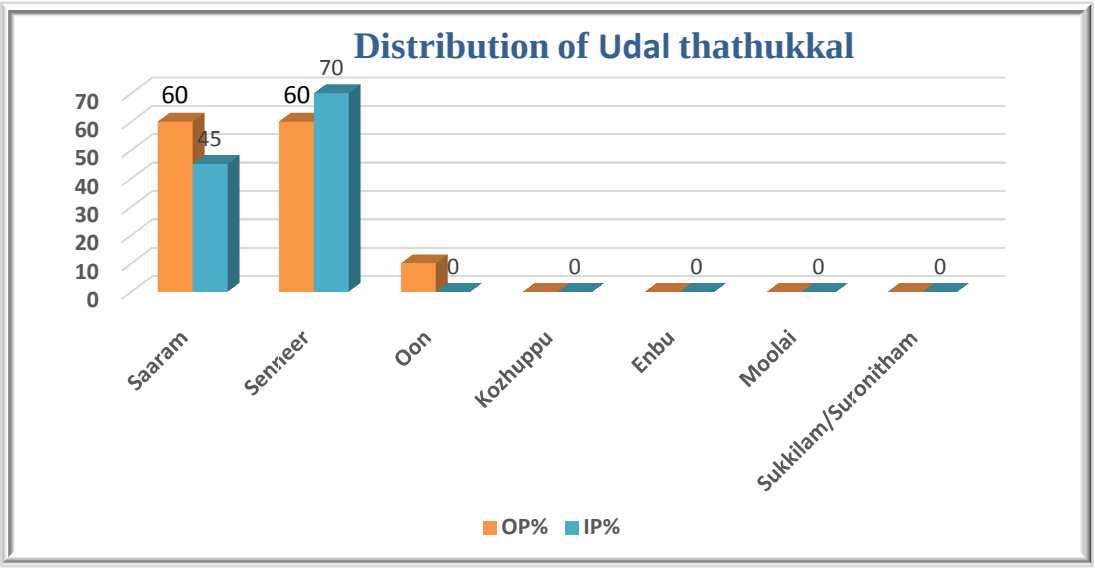
Above Table-V.2.20 and Figure-V.2.20 showed that among 20 OP, Pranan was affected in 60% cases, Abanan was affected in 100% cases, Vyanan was affected in 40% ,samanan was affected in 50,Kirukaran was affected in 50%,Devadathan was affected in 60%,Analagam was affected in 60%,Ranjagam was affected in 60%,Sathagam was affected in 40%,Kilethagam was affected in 60%. Among 20 IP Abanan was affected in 100% cases, Pranan was affected in 45% cases, Vyanan was affected in 30%, samanan was affected in 60%,Kirukaran was affected in 45%, Devadathan was affected in 45%,Analagam was affected in 50%,Ranjagam was affected in 70%,Sathagam was affected in 35%,Kilethagam was affected in 70%,

V.2.21: Distribution of Udal thathukkal

Table-V.2.21: Distribution of Udal thathukkal

Udal thathukkal	OP		IP	
	No of cases	%	No of cases	%
Saaram	12	60	9	45
Senneer	12	60	14	70
Oon	2	10	-	-
Kozhuppu	-	-	-	-
Enbu	-	-	-	-
Moolai	-	-	-	-
Sukkilam/Suronitham	-	-	-	-

Figure-V.21: Distribution of Udal thathukkal



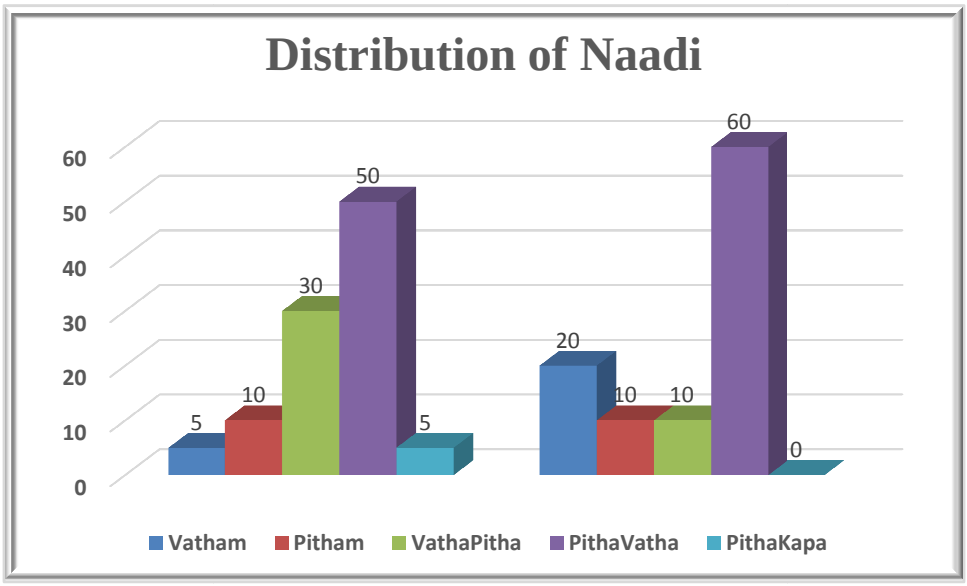
Above Table -V.2.21 and Figure- V.2.21 showed that among. Among 20 OP, saaram was affected in 60% cases, senneer was affected in 60% cases, among 20 IP saaram was affected in 45% cases, senneer was affected in 70% cases.

V.2.22: Distribution of Naadi

Table-V.2.22: Distribution of Naadi

Naadi	OP		IP	
	No of cases	%	No of cases	%
Vatham	1	5	4	20
Pitham	2	10	2	10
VathaPitha	6	30	2	10
PithaVatha	10	50	12	60
PithaKapa	1	5	0	0
Total	20	100	20	100

Figure : V.2.22: Distribution of Naadi



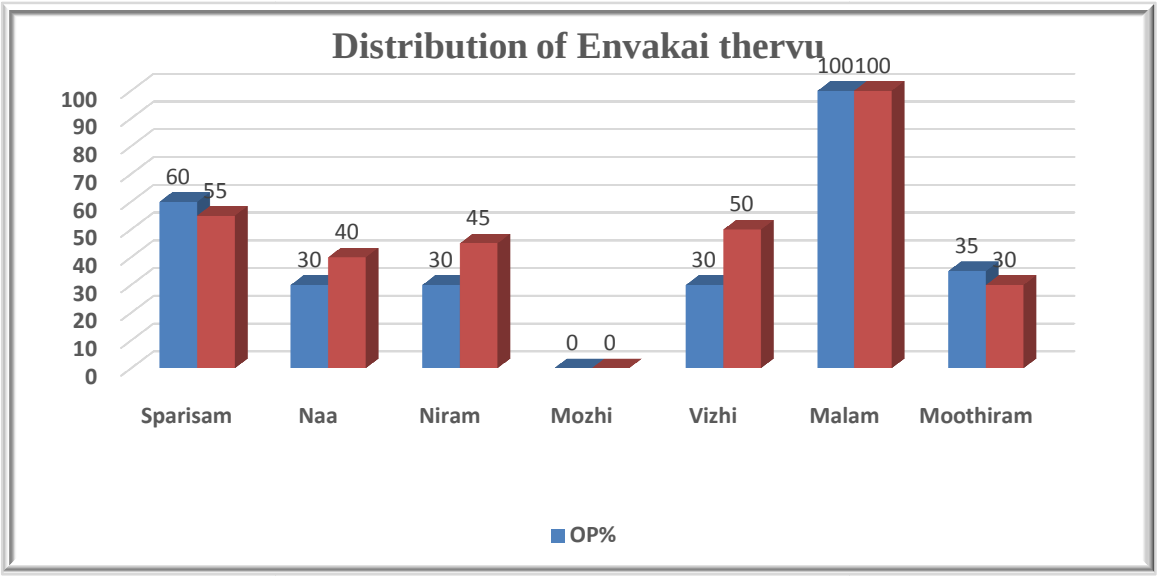
Above Table -V.2.22 and Figure- V.2.22 showed that among 20 OP 50% were having Pithavatha naadi 30% were having Vathapitha naadi, 10% were having Pitha naadi and amoung 20 IP cases, 60% were having Pithavatha naadi 20% were having Vatha naadi, 10% were having Pitha naadi & Vathapitha naadi.

V.2.23: Distribution of Envakai thervu

Table-V.2.23: Distribution of Envakai thervu

Envagai thervu	OP		IP	
	No of cases	%	No of cases	%
Sparisam	12	60	11	55
Naa	6	30	8	40
Niram	6	30	9	45
Mozhi	-	-	-	-
Vizhi	6	30	10	50
Malam	20	100	20	100
Moothiram	7	35	6	30

Figure-V.2.23: Distribution of Envakai thervu



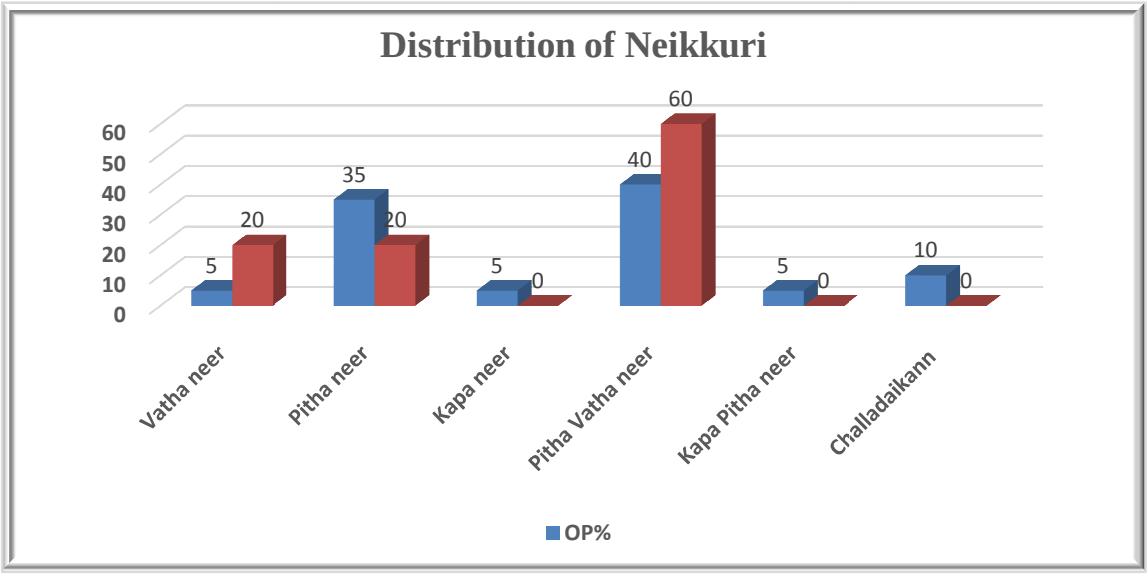
Above Table-V.2.23 and Figure-V.2.23 showed that among 20 OP cases Sparism was affected in 60%, Naa was affected in 30%, niram was affected in 30%, Vizhi was affected in 30%, Malam was affected in 100%, Moothiram was affected in 35%. Among 20 IP cases Sparism was affected in 55%, Naa was affected in 40%, niram was affected in 45%, Vizhi was affected in 50%, Malam was affected in 100%, Moothiram was affected in 30%.

V.2.24: Distribution of Neikkuri

Table-V.2.24: Distribution of Neikkuri

Neikkuri	OP		IP	
	No of cases	%	No of cases	%
Vatha neer	1	5	4	20
Pitha neer	7	35	4	20
Kapa neer	1	5	0	0
Pitha Vatha neer	8	40	12	60
Kapa Pitha neer	1	5	0	0
Challadaikann	2	10	0	0
Total	20	100	20	100

Figure-:V.2.24: Distribution of Neikkuri



Above Table -V.2.24 and Figure- V.2.24showed that among 20 OP cases, 5% were having Vatha neer, 35% were having Pitha neer, 40% were having Pitha vatha neer, 5% were having Kapa neer & Kapapitha neer. Among 20 IP population, 20% were having vathaneer, 20% were having pithaneer, 60% were Pithavathaneer.

V.2.25: Distribution of Clinical presentation

Table-V.2.25: Distribution of Clinical presentation and its Percentage

Parameter	OP	%	IP	%
Classical:7 Criteria	1	5	5	25
Confirmative:6 Criteria	2	10	4	20
Clinical:5 Criteria	12	60	7	35
Diagnostic:4Criteria	3	15	4	20
Suggestive:3Criteria	2	10	0	0

Figure-V.2.25: Distribution of clinical presentation

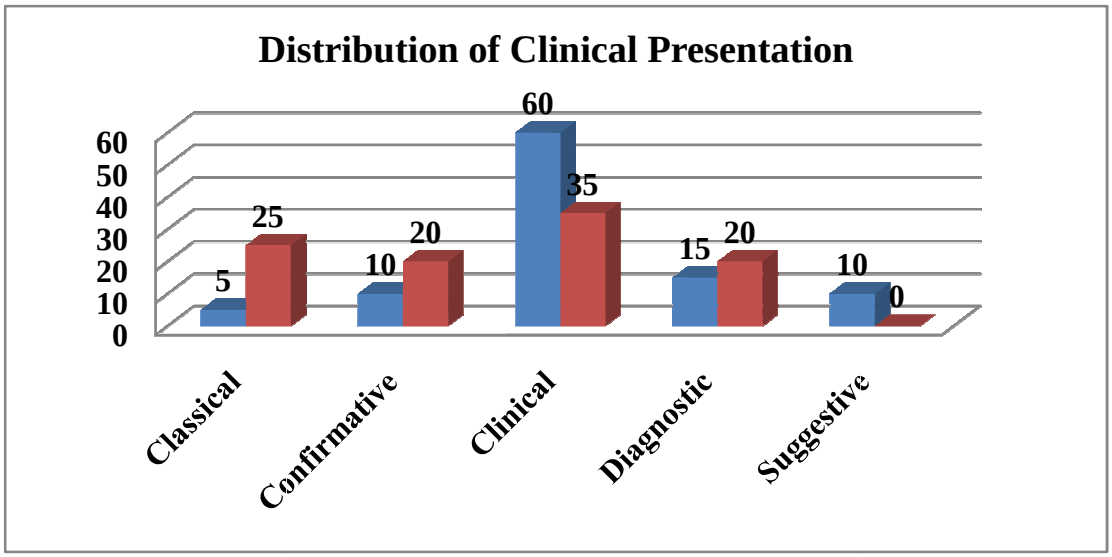


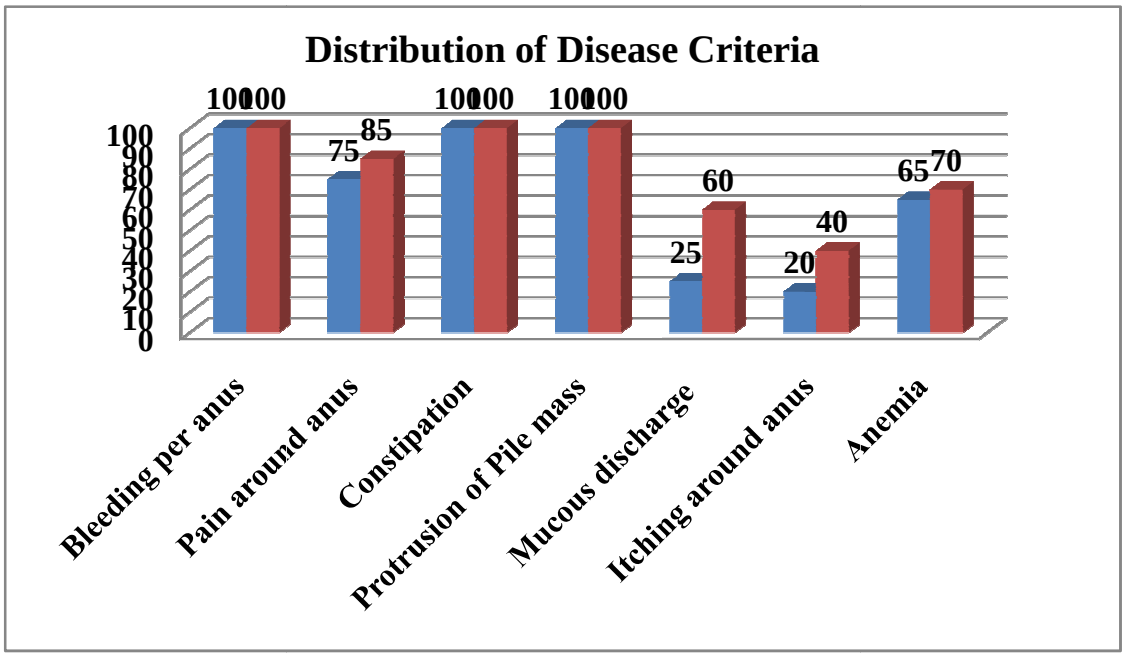
Table-V.2.25 and Figure-V.2.25 showed that 60% cases of clinical presentation were according to clinical criteria in OP and 15% cases of clinical presentation were according to diagnostic criteria and 10% according to confirmative and suggestive criteria respectively. 35% cases of clinical presentation were according to Clinical criteria and 25% cases were according to classical and 20% cases according to diagnostic criteria among IP cases.

V.2.26: Distribution of Disease criteria

Table-V.2.26: Distribution of Disease criteria

Disease criteria	OP		IP	
	No of cases	%	No of cases	%
Bleeding per anus	20	100	20	100
Pain around anus	15	75	17	85
Constipation	20	100	20	100
Protrusion of Pile mass	20	100	20	100
Mucous discharge	5	25	12	60
Itching around anus	4	20	8	40
Anemia	13	65	14	70

Figure-V.2.26: Distribution of Disease criteria



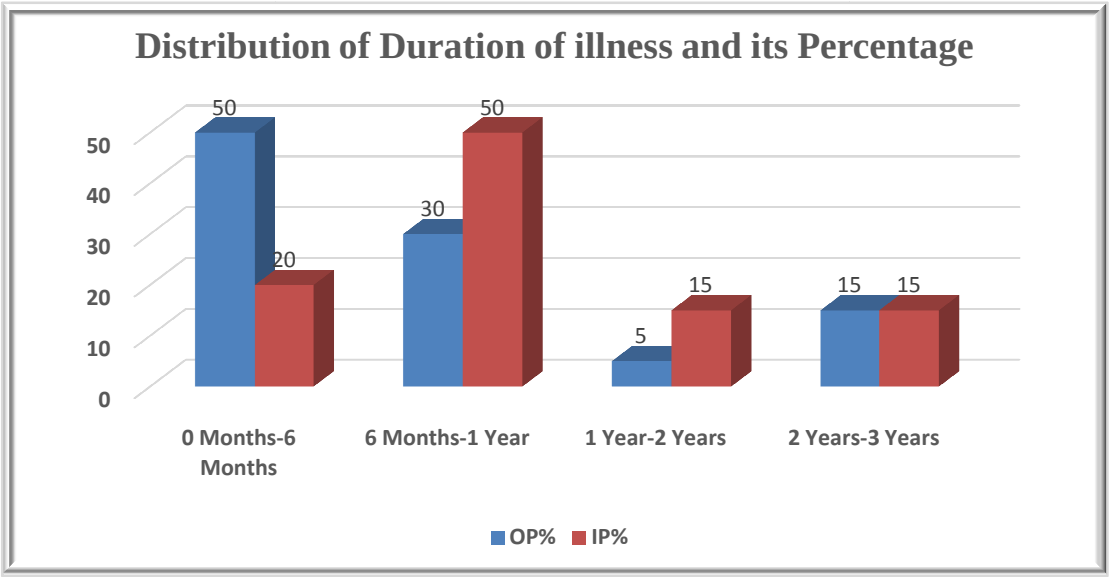
Above Table-V.2.26 and Figure-V.2.26 revealed that high prevalence of symptoms were Bleeding per anus, Constipation and Protrusion of pile mass in Rathamoolam (100%).

V.2.27: Distribution of Duration of illness

Table-V.2.27: Distribution of Duration of illness and its Percentage

Duration of illness	OP		IP	
	No of cases	%	No of cases	%
0 Months-6 Months	10	50	4	20
6 Months-1 Year	6	30	10	50
1 Year-2 Year	1	5	3	15
2 Year-3 Year	3	15	3	15
Total	20	100	20	100

Figure-:V.2.27: Distribution of Duration of illness



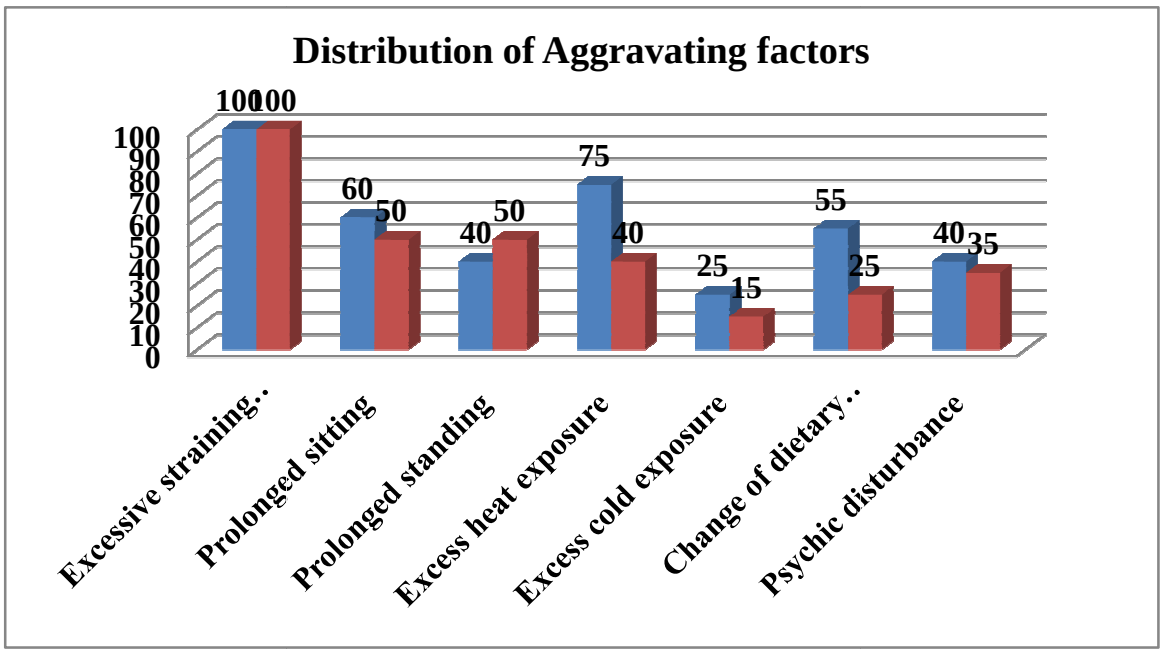
Above Table-V.2.27 and Figure-V.2.27 showed that among 40 patients, out of 20 OP 50% patients were suffering from six months, 30% were suffering from one year, 5% were suffering from two years, 15% were suffering from three years. Out of 20 IP 20% patients were suffering from six months, 50% were suffering from one year, 15% were suffering from two years,15% were suffering from three years.

V.2.28: Distribution of Aggravating factors of Rathamoolam

Table-V.2.28: Distribution of Aggravating factors of Rathamoolam

Aggravating factors of Rathamoolam	OP		IP	
	No of cases	%	No of cases	%
Excessive straining at stool	20	100	20	100
Prolonged sitting	12	60	10	50
Prolonged standing	8	40	10	50
Excess heat exposure	15	75	8	40
Excess cold exposure	5	25	3	15
Change of dietary habits	11	55	5	25
Psychic disturbance	8	40	7	35

Figure-V.2.28: Distribution of Aggravating factors of Rathamoolam



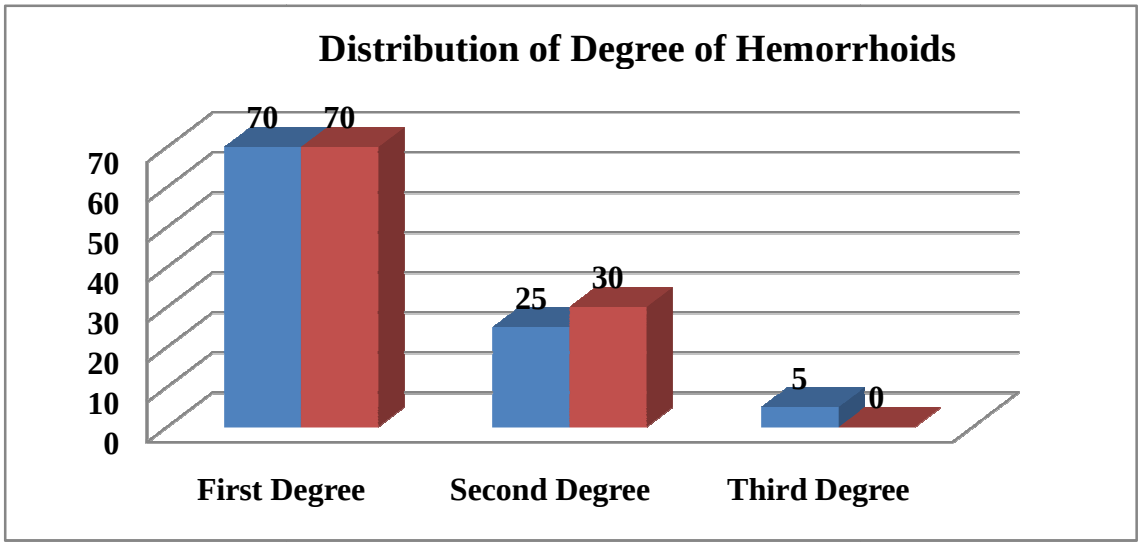
Above Table-V.2.28and Figure-V.2.28 revealed that Excessive Straining at stool (100%) and Excess heat exposure (75%) have high prevalence in aggravating Rathamoolam among 20 OP cases. In IP cases 100% is due to Excessive straining at stool and 50% is due to prolonged sitting and prolonged standing respectively.

V.2.29: Distribution of Degree of Hemorrhoids

Table-V.2.29: Distribution of Degree of Hemorrhoids

Degree of Hemorrhoids	OP		IP	
	No of cases	%	No of cases	%
First Degree	14	70	14	70
Second Degree	5	25	6	30
Third Degree	1	5	0	0

Figure-V.2.29: Distribution of Degree of Hemorrhoids



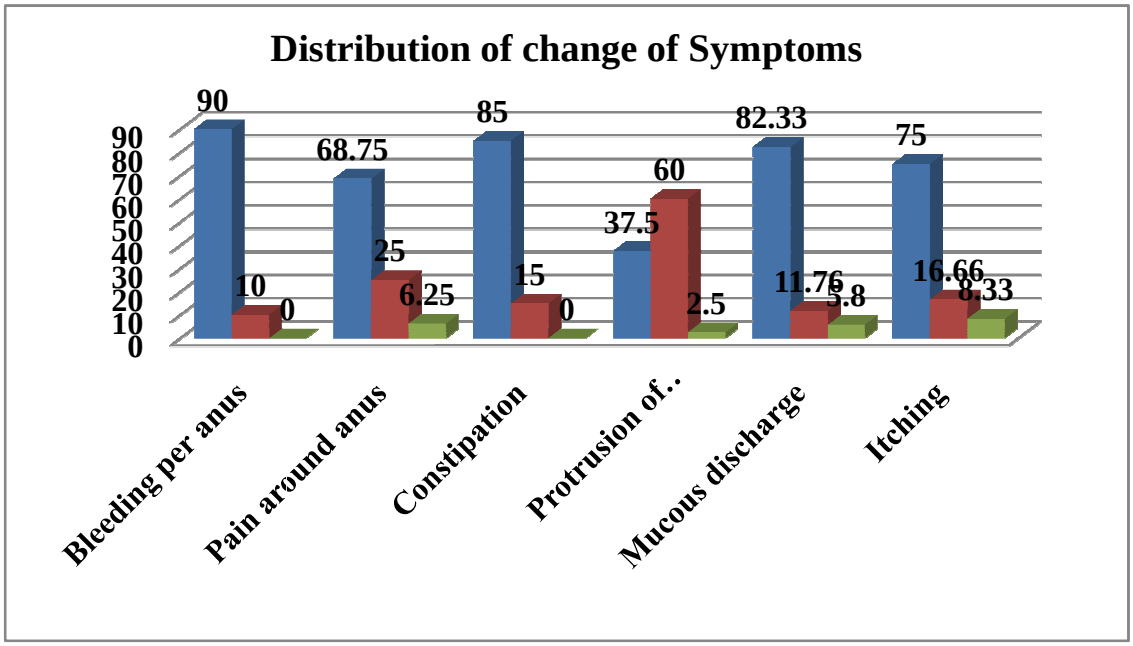
Above Figure-V.2.29&Table-V.2.29 showed that among 40 patients, Out of 20 OP 70% of cases had First degree hemorrhoids, 25% of cases had second degree hemorrhoids, 5% of cases had third degree hemorrhoids. Out of 20 IP 70% of cases had First degree hemorrhoids, 30% of cases had second degree hemorrhoids.

V.2.30: Distribution of Change of Symptoms

Table-V.2.30: Distribution of change of symptoms

Symptoms	Number of cases	Resolved	%	Good improvement	%	Poor	%
Bleeding per anus	40	36	90	4	10	-	-
Pain around anus	32	22	68.75	8	25	2	6.25
Constipation	40	34	85	6	15	-	-
Protrusion of pilemass	40	15	37.5	24	60	1	2.5
Mucous discharge	17	14	82.33	2	11.76	1	5.8
Itchy anus	12	9	75	2	16.66	1	8.33

Figure-V.2.30: Distribution of Change of Symptoms



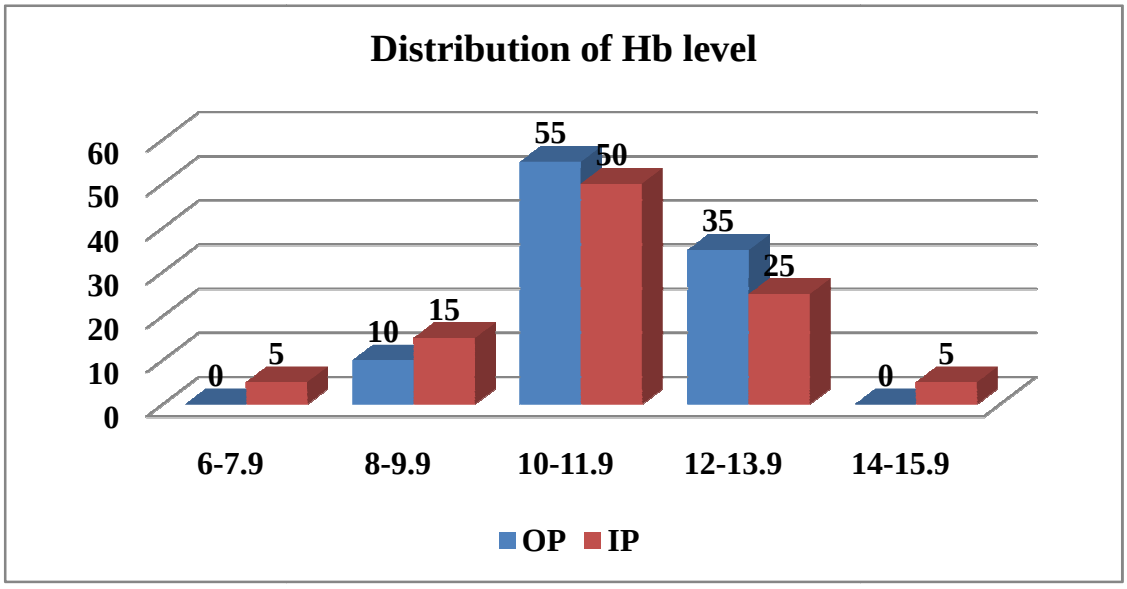
Above Table-V.2.30 & Figure-V.2.30 revealed that 90% of cases had good improvement in bleeding per anus symptom among 40 patients, 68.75% of cases had good impovemet in pain around anus symptom among 32 patients, 85% of cases had good impovemet in constipation symptom among 40 patients, 37.5% of cases had good impovemet in protrusion of pile mass symptom among 40 patients, 82.33% of cases had good impovemet in mucous discharge symptom among 17 patients, 75% of cases had good impovemet in itching around anus symptom among 12 patients.

V.2.31: Distribution of Hb level

Table-V.2.31: Distribution of Hb level

Hb level (gm/dl)	OP		IP	
	No of cases	%	No of cases	%
6-7.9	0	0	1	5
8-9.9	2	10	3	15
10-11.9	11	55	10	50
12-13.9	7	35	5	25
14-15.9	0	0	1	5

Figure-V.2.31: Distribution of Hb level



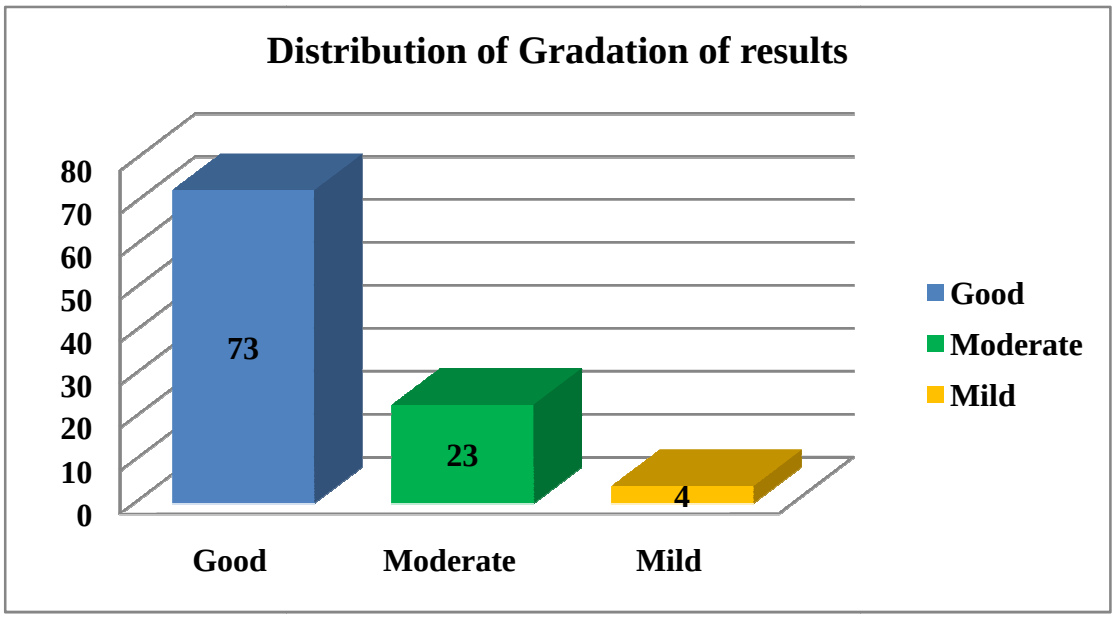
Above Table-V.2.31 & Figure-V.2.31 showed that among 40 patients, out of 20 OP 55% cases had Hb level in between the range 10-11.9, 35% cases had in between the range 12-13.9, 10% of cases had in between the range 8-9.9. Out of 20 IP 50% cases had Hb level in between the range 10-11.9, 25% cases had in between the range 12-13.9. 15% cases had Hb level in between the range of 8-9.9.

V.2.32: Distribution of Gradation of results

Table-V.2.32: Distribution of Gradation of results

Gradation of Results	Percentage
Good	73
Moderate	23
Mild	4

Figure-V.2.32: Distribution of Gradation of results



Above Table-V.2.32 &Figure-V.2.32 showed that among 40 patients 73% of patients had good improvement, 23% had moderate improvement and 4% had mild improvement.

CHAPTER-VI

DISCUSSION

The Rathamoolam is correlated to Bleeding hemorrhoid in Modern science. The types of Moolam, its name, etiology, pathogenesis, clinical features, prognosis and treatments etc are being discussed in the review of literature in siddha aspect. The modern aspects of Hemorrhoid which include Anatomy, physiology, pathology and treatments are also discussed in review chapter.

In this trial, 40 cases of Rathamoolam patients who attended the OPD and IPD of GSMC, Palayamkottai were selected according to Protocol. The screened and selected patients were treated with the Trial medicine Nelli kudineer. Preclinical study of NK including Biochemical,Phytochemical,Anti microbial,Pharmacological and Toxicity studies also done and proven for its therapeutic uses for Rathamoolam. Clinical assessment was carried out before and after the treatment with NK. From my trial following findings were observed and discussed.

VI.1. SIDDHA ASPECT OF NK FOR RATHAMOOLAM

In Rathamoolam	V↑, P↑, Neer↓	
Line of treatment	To normalize ↑V,↑ P, ↓ Neer	
Vatham normalized by	Sweet, Sour, Salt	
Pitham normalized by	Sweet, Astringent, Bitter	
Method of preparation	Ekamoolikai prayokam	
GUNAM (PROPERTIES OF NK)		
Suvai: Taste	Sweet : Mann+ Neer	Activate 5 sense organs
	Sour : Mann+ Theyu	Proper digestion Easy defecation Nourishes blood vessels
	Astringent: Mann+ Vaayu	Constricting effect
Veeriyam: Potency	Cold	Removes Pitham& Ratham ↑ Life span Give pleasure to mind
Pirivu:Post absorptive taste	Sweet : Mann+ Neer	Neer bootham maintained
Predominent bootham	Mann	Evacuate the thodam within the intestine by defecation Has qualities of other bootham
Interpretation	**Gunam of NK normalizes the vitiated Vatham& Pitham, Neer bootham attained to its normal level, thereby reduced the symptoms of RM. So, Nelli Kudineer is effective for the treatment of Rathamoolam.**	

VI.2. PRE CLINICAL STUDY OF NK

Pre clinical study	**Inference** (+) Present / (-) absent	**Interpretation**
Biochemical analysis	Calcium(+)	*Blood clotting*
	Sulphate(+)	*Increases stool mass*
	Chloride(+)	*Keep the fluid amount inside &outside of cells*
	Ferrous iron(+)	*Synthesis of Hb*
	Tannic acid(+)	*Astringent principle, coagulate the protein in the skin& protect it.Reduces Inflammation, itching, mucous discharge around anus.*
	Unsaturated compounds(+)	Carryout addition reactions, More reactive
	Amino acids(+)	Ascorbic acid is highly stable; stability is attributed to Tannins & Poly phenols which retard the oxidation of ascorbic acid.
Phytochemical analysis	Alkaloids(+)	Anti microbial activity
	Phenols(+)	Anti oxidant property
	Glycosides(+)	Anti viral activity
	Steroids(+)	----------
	Tannins(+)	*Astringent, Anti inflammatory, Anti infective, Anti oxidant.*
	Terpenoids(+)	*Anti inflammatory.*
Anti microbial assay	Anti microbial activity(+) Staphylococcus aureus,E.coli (ZIC 13,14 mm resply)	*Anti infective*
Pharmacological study	***Anti coagulant action***(+)	*Arrest bleeding*
	Laxative action(+)	*Relieves Constipation*
	Analgesic action(+)	*Relieves Pain around anus*
	Anti inflammatory action(+)	*Subsiding inflammation around anus*
	Haematinic activity(+)	*increases Hb level*
Toxicity study	Acute toxicity(-)	*No morbidity& mortality*
	Chronic toxicity(-)	*No evidence of severe Toxicity*

VI.3.CLINICAL STUDY OF NK FOR RATHAMOOLAM

Distribution		Prevalence	
		OP	IP
Gender	M	**50**	15
	F	50	**85**
Age (Yr)	21-30	30	10
	31-40	20	20
	41-50	**35**	10
	51-60	15	**60**
Religion	Hindu	**60**	**90**
	Muslim	25	0
	Christian	15	10
Educational Status	Mid. School	10	25
	High School	30	**60**
	College	**35**	10
Occupation	Housewife	20	30
	Student	15	0
	Labourer	30	**45**
	Sedentary	**35**	25
Socio Economic Status	Upper	20	0
	Middle	**50**	40
	Lower	30	**60**
Marital Status	Married	**65**	**95**
	Unmarried	35	5
Family H/O Hemorrhoids	Yes	**40**	**30**
	No	60	70
Dietary Habits	Veg	25	10
	Mixed	**75**	**90**
	Timely	20	15
	Untimely	**80**	**85**
Addiction	Smoking	15	10
	Alcohol	10	5
	Tobacco	15	10
	Coffee	40	45
	Tea	**60**	**55**
Sleep	Normal	**65**	**50**
	Disturbed	30	**50**
Previous Treatment	Yes	**30**	**40**
Nilam	Kurinchi	5	0
	Marutham	**75**	**65**
	Neithal	20	35

Kaalam		Kaar	10	15
		Koothir	15	**30**
		Munpani	5	20
		Pinpani	5	20
		Ilavenil	**35**	4
		Mudhuvenil	30	10
Theki		VP	40	35
		PV	**45**	**50**
		PK	10	5
Gunam		Rajas	**100**	**100**
Kanmenthiriyam		Eruvai	**100**	**100**
Aasayangal		Amarvasayam	60	45
		Pakirvasayam	35	25
		Malavasayam	**100**	**100**
Kosangal		Annamayam	**60**	**60**
		Piranamayam	40	40
Uyir thathukkal	Vatham	Pranan	60	45
		Abanan	**100**	**100**
		Viyanan	40	30
		Samananan	50	60
		Kirukiran	60	45
		Devathathan	60	45
	Pitham	Analakam	**60**	50
		Ranjakam	**60**	**70**
		Sathakam	40	35
	Kapam	Kilethakam	**60**	**70**
Udal thathukkal		Saaram	**60**	45
		Senneer	**60**	**70**
Naadi		V	5	20
		P	10	10
		VP	30	10
		PV	**50**	**60**
		PK	5	0
Envakai Thervu		Sparisam	**60**	**55**
		Naa	30	40
		Niram	30	45
		Vizhi	**30**	**50**
		Malam	**100**	**100**
		Moothiram	35	30
Neikkuri		V	5	20
		P	35	20
		K	5	0
		PV	**40**	**60**
		KP	5	0
		Challadai	10	0

Clinical Presentation	Classical	5		25
	Confirmative	10		20
	Clinical	**60**		**35**
	Diagnostic	15		20
	Suggestive	10		0
Disease Criteria	Bleeding per anus	**100**		**100**
	Pain around anus	**75**		**85**
	Constipation	**100**		**100**
	Prolapse of pilemass	**100**		**100**
	Mucous discharge	25		60
	Itching	20		40
	Anemia	65		70
Duration of Illness	0 M – 6 M	**50**		20
	6 M – 1 Y	30		**50**
	1 Y – 2 Y	5		15
	2 Y – 3 Y	15		15
Aggravating Factors	Excess straining at stool	**100**		**100**
	Prolonged sitting	**60**		**50**
	Prolonged standing	40		**50**
	Excess heat exposure	**75**		40
	Excess cold exposure	25		15
	Change of dietary habit	55		25
	Psychic disturbances	40		35
Degree of Hemorrhoids	First	**70**		**70**
	Second	25		30
	Third	5		0
Hb level (gm/dl)	6-7.9	0		5
	8-9.9	10		15
	10-11.9	**55**		**50**
	12-13.9	35		25
Change of Symptoms	Symptoms	***Good***	***Mod***	***Mild***
	Bleeding per anus	**90**	**10**	**0**
	Pain around anus	**68.75**	**25**	**6.25**
	Constipation	**85**	**15**	**0**
	Prolapse of pilemass	**37**	**60**	**2.5**
	Mucous discharge	**82.35**	**11.76**	**5.88**
	Itching	**75**	**16.66**	**8.33**
Gradation of results	***Good***	***73***		
	Moderate	***23***		
	Mild	***4***		

VI.4.STATISTICAL ANALYSIS : PRECLINICAL STUDY

Results are reported as mean ± S.E.M. The Statistical Analysis were performed using one way analysis of variance(ANOVA). For tests, differences with value of P<0.05 (P-value) were considered significant

Anticoagulant activity	Significant reduction in cloting profile	P < 0.01
Laxative action	Significant dose dependent increase in faeces output	P<0.01
Analgesic action	Significant analgesic ativity in animal model of pain	P<0.01
Anti inflammatory action	Significant anti inflammatory activity	P<0.01
Haematinic action	Signifiant increase in Hb level	P<0.01

VI.4.STATISTICAL ANALYSIS : CLINICAL STUDY

Data were expressed as mean and SD. The significance of the difference between before (BT) and after treatement (AT)was tested using Paired 't' test. A probability value (P-value) of <0.05 was considered to be statisitically significant.

Grade	BT & AT	MEAN	STANDARD DEVIATION	t VALUE	P VALUE
Bleeding per anus	BT	1.82	0.874	12.599	< 0.05
	AT	0.13	0.335		
Pain around anus	BT	1.13	0.791	6.985	< 0.05
	AT	0.28	0.452		
Constipation	BT	1.48	0.506	15.943	< 0.05
	AT	0.15	0.362		
Protrusion of Pile mass	BT	1.33	0.526	7.286	< 0.01
	AT	0.62	0.540		
Mucous Discharge	BT	0.45	0.552	5.152	< 0.01
	AT	0.00	0.000		
Itchy anus	BT	0.35	0.580	3.819	< 0.01
	AT	0.00	0.000		
Haemoglobin	BT	11.183	1.5377	-1.771	< 0.01
	AT	11.340	1.2989		

CHAPTER-VII

SUMMARY

The clinical study on Rathamoolam (bleeding Hemorrhoids) consisting of 40 patients were treated by trail drug Nelli Kudineer 100ml OD morning has been evaluated based on pre clinical, clinical and Siddha aspects. High prevalence of symptoms in RM were Bleeding per anus, Constipation and Protrusion of pile mass. Excessive Straining at stool , Excess heat exposure, prolonged sitting had high prevalance in aggravating the Rathamoolam. After treatment there was good improvement in symptoms of bleeding per anus and constipation (90% and 85% respectively), mucous discharge and itchy anus (82% and 75% respectively).Significant increase in Hb level at the 0.01 level (2-tailed). The gradation of result was found to be good improvement in 73% cases, moderate improvement in 23% cases and mild improvement in 4% cases. None of them required any treatment for adverse events. There were no serious adverse and unexpected events reported during my clinical trial. The NK proved to be safe clinically.

Preclinical study of Nelli Kudineer revealed the presence of following bio chemicals calcium, sulfate, ferrous iron, tannic acid, unsaturated compound and amino acid. Presence of **Tannic acid** in NK has an Astringent Principle, which coagulate the protein in skin and protect the tissue by forming a thin layer. It also decreases the Mucous and other secretion and there by decreasing inflammation and irritation around the anal area and also provide relief from burning and itching but not pain. Phytochemical analysis revealed the presence of alkaloids, phenols, glycosides, steroids, tannins and terpenoids. Many human physiological activities such as stimulation of phagocytic cells, host-mediated tumor activity and anti-infective actions assigned to tannins. Phenols act through the mechanism of substance deprivation and terpenoids act through the membrane disruption. Pharmacological studies of NK proved the styptic ($P<0.01$), laxative ($P<0.01$) analgesic ($P<0.01$), anti-inflammatory ($P<0.01$) and hemetenic activity ($P<0.01$). Acute and chronic toxicity study of NK in animals showed no morbidity and mortality. Effect of NK on haemetolical parameters of Hb showed significant increase in Hb level ($P<0.01$). Thus above mentioned preclinical study proved that NK is good for the management of Rathamoolam.

Vatha Pitha thontha deranged Rathamoolam (RM) is normalized by sour, astringent, sweet taste of NK. The Cold potency (thatpam) of NK acts on RM by eliminating excess pitham. The post absorptive taste (pirivu) of NK is sweet (inippu). Vatham and pitham are also normalized by sweet taste. Mann (earth) is predominant bootha in NK which evacuate the thodam within the intestine by defection there by it improved the function of abanavaayu, which regulate the bowel habits and lead to normal functioning of udal thathus. **Gunam of NK normalizes the vitiated Vatham& Pitham, Neer bootham attained to its normal level, thereby reduced the symptoms of RM. So,the trial summerised that Nelli Kudineer is effective for the treatment of Rathamoolam.**

CHAPTER-VIII

CONCLUSION

My thesis prospective open labelled phase-II non randomized clinical study of Nelli Kudineer (NK) for Rathamoolam (RM) in modern science bleeding hemorrhoids concluded the clinical and therapeutic efficacy of NK for RM by showing improvement in grades of symptoms. No adverse events were reported during the clinical study, the trial drug appears to be safe. The pre clinical studies including bio chemical, Phytochemical, anti microbial and pharmacological evaluation revealed the presence of various bio chemicals, phytochemicals and showed good styptic, laxative, anti inflammatory and haemetenic action.The acute and chronic toxicity study showed the good safety profile of NK. The panchabootham, taste, potency and post absorptive taste (pirivu) of NK was found to correct the deranged humors there by regulizing the udal thathus and proved the effective management of RM.

Bio statistical analysis of pharmacological study showed the significant styptic action (P value<0.01), laxative action (P value<0.01), analgesic action (P value<0.01), anti inflammatory (P value<0.01), haemetenic action (P value<0.01). NK showed significant degrees in plasma cholesterol, TG, LDL (P value<0.05), significant increase in HDL cholesterol (P value<0.05). AST, ALT, ALP levels were normal in NK treated animals (P value<0.05). NK showed the significant increase in Hb level (P value<0.01).

The clinical manifestations (bleeding, pain, constipation, protrusion of pilemass) of RM before treatment and after treatment is statistically significant (P<0.05). Other manifestations (Mucous discharge, itching) also statistically significant (P<0.01). The clinical studies in both OP & IP were motivating and gave hope in the management of RM. The gradation of result was found to be good improvement in 73% cases, moderate improvement in 23% cases and mild improvement in 4% cases.

This is only a preliminary study and by understanding limitations from this study, elaborate study will be undertaken to assess the further more effect of NK. Siddha way of approach is certainly the best treatment of RM in all aspects, because of encouraging results clinically and pre clinically, it is concluded that RM is manageable with NK.

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ANNEXURE

ANNEXURE-I

1.SCREENING COMMITTEE APPROVAL

GOVERNMENT SIDDHA MEDICAL COLLEGE
PALAYAMKOTTAI

SCREENINGCOMMITTEE

Name of the Candidate : Dr. M.Sumayya.

Registration No. of the Candidate:.....

DEPARTMENT OF POTHUMARUTHUVAM

This is to certify that the dissertation topic *"A Prospective Open labelled Phase II Randomized clinical study of* ***NELLI KUDINEER for RATHAMOOLAM"*** has been approved by the screening committee.

Branch	Department	Name	Signature
1	Pothu Maruthuvam	Dr.A.Manoharan. MD(S) Professor	
2	Gunapadam	Dr.A.Kingsly MD(S) Associate Professor	
3	Sirappu Maruthuvam	Dr.A.S.Poongodi Kanthimathi MD(S) Professor	
4	Kuzhandhai Maruthuvam	Dr.D.K.Soundararajan. MD(S) Professor	
5	Noi Nadal	Dr.S.Victoria MD(S) Professor	
6	Nanju Nool Maruthuvam	Dr.M.Thiruthani. MD(S) Professor	

Place : Palayamkottai

Date : 26.05.2017

PRINCIPAL
Govt. Siddha Medical College
Palayamkottai

ANNEXURE-I

2. IEC CERTIFICATE OF APPROVAL

INSTITUTIONAL ETHICAL COMMITTEE,
GOVERNMENT SIDDHA MEDICAL COLLEGE,
PALAYAMKOTTAI, TIRUNELVELI- 627002,
TAMIL NADU, INDIA.

Ph: 0462-2572736/2572737/2582010 Fax: 0462-2582010
Email ID: gsmc.palayamkottai@gmail.com

R.No. GSMC/5676/P&D/Res/IEC/2014 **Date: 29.05.2017**

CERTIFICATE OF APPROVAL

Address of Ethical Committee	Government Siddha Medical College, Palayamkottai-627002, Tirunelveli district.
Principal Investigator	Dr. M. SUMAYYA MD(s), First year, Department of Pothu Maruthuvam, Reg. No: Not yet registered.
Supervisor & Guide	**Prof.Dr.A.Manoharan, M.D(S),** Head of the Department, Department of Pothu Maruthuvam, Government Siddha Medical College and Hospital, Palayamkottai - 627002, Tirunelveli District. drmanoharan25@gmail.com
Dissertation Topic	*A Prospective open labelled Phase II Non Randomized clinical study of* ***Nelli Kudineer for Rathamoolam*** *(BLEEDING HAEMORRHOIDS)*
Documents Filed	(1)Protocol (2)Data Collection Forms (3)Patient Information Sheet (4)Consent Form (5)SAE (Pharmacovigilance)
Clinical/Non Clinical Trial Protocol (Others-Specify)	Clinical Trial Protocol-yes
Informed Consent Document	Yes
Any other Document	Case Sheet/Investigation Documents
Date of IEC Approval & its Number	**29-05-2017 & GSMC-IV-IEC/2017/Br-I/10**

. We approve the trial to be conducted in its presented form.

The Institutional Ethical Committee expects to be informed about the process report to be submitted to the IEC at least annually of the study, any SAE occurring in the course of the study, any changes in the protocol and submission of final report.

Chairman

Prof. Dr. M. MURUGESAN. MD(S)

Member Secretary

29/5/17

Prof Dr.R.NEELAVATHY.MD(S) Ph.D.

ANNEXURE-II

IAEC CERTIFICATE

K.M. COLLEGE OF PHARMACY – MADURAI

IAEC – CERTIFICATE

This is to certificate that the project title A PROSPECTIVE OPEN LABELLED PHASE II NON RANDOMIZED CLINICAL STUDY OF **"NELLI KUDINEER" FOR "RATHAMOOLAM" (BLEEDING HAEMORRHOID)** has been approved by the **IAEC/ M. SUMAYYA /TNMGRMU/MD(S)/ 321611010/KMCP/29/2018.**

Dr. K. CHIDAMBARANATHAN
Name of the Chairman / Member Secretary IAEC:

Dr. P. THANGAPANDI KUMARESAN
Name of the CPCSEA Nominee

Signature with Date 11/5/18

I. A. E. C. CHAIRMAN
INSTITUTIONAL ANIMAL ETHICAL COMMITTEE
K. M. COLLEGE OF PHARMACY
MADURAI-625 107.

11/5/18
CPCSEA NOMINEE
INSTITUTIONAL ANIMAL ETHICS COMMITTEE
K.M. COLLEGE OF PHARMACY
MADURAI-625 107

Chairman / Member Secretary of IAEC **CPCSEA Nominee**

(Kindly make sure that minutes of the meeting duly signed by all the participants are maintained by office).

ANNEXURE-III

CTRI REGISTRATION CERTIFICATE

Clinical Trial Details (PDF Generation Date :- Thu, 29 Mar 2018 09:29:56 GMT)

CTRI Number	CTRI/2018/03/012713 [Registered on: 21/03/2018] - **Trial Registered Prospectively**
Last Modified On	23/02/2018
Post Graduate Thesis	Yes
Type of Trial	Interventional
Type of Study	Siddha
Study Design	Single Arm Trial
Public Title of Study	A clinical study to study the effect of drug NELLI KUDINEER in RATHAMOOLAM(Bleeding Haemorrhoids)
Scientific Title of Study	A Prospective Open Labelled Phase II Non Randomized clinical study of NELLI KUDINEER for RATHAMOOLAM(Bleeding Haemorrhoids)

Secondary IDs if Any

Secondary ID	Identifier
NIL	NIL

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Details of Principal Investigator	
Name	Sumayya M
Designation	PG student
Affiliation	Govt Siddha Medical College and hospital Palayamkottai
Address	PG second year Department of Pothumaruthuvam Govt Siddha Medical College and hospital Palayamkottai Tirunelveli Tamilnadu Tirunelveli TAMIL NADU 627002 India
Phone	9746242799
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Details Contact Person (Scientific Query)

Details Contact Person (Scientific Query)	
Name	Prof Dr A Manoharan MD
Designation	Head of Department Department of Pothumaruthuvam
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Details Contact Person (Public Query)	
Name	Prof Dr A Manoharan MD
Designation	Head of Department Department of Pothumaruthuvam
Affiliation	Govt Siddha Medical College and hospital Palayamkottai
Address	Head of Department Department of Pothumaruthuvam Govt Siddha Medical College Palayamkottai Tirunelveli Tamilnadu Tirunelveli TAMIL NADU 627002 India

ANNEXURE-IV

CERTIFICATE OF BOTANICAL AUTHENTICITY

GOVERNMENT SIDDHA MEDICAL COLLEGE
PALAYAMKOTTAI

Certificate of Botanical Authenticity

Certified the following plant drug used in Siddha formulation (Internal) **"NELLI KUDINEER"** for **RATHAMOOLAM** (BLEEDING HAEMORRHOIDS) taken up for Post-Graduation Dissertation Studies by Dr.M.SUMAYYA, PG Scholar MD siddha, Department of Pothu Maruthuvam, are correctly identified and authenticated through Visual inspection / Organoleptic Characters / Experience, Education & Training Morphology Microscopically and Taxonomical methods.

Table 1: Ingredients of Nelli Kudineer

S.N	Drug	Botanical Name	Family	Parts Used
01	Nelli	*Phyllanthus emblica, Linn*	Euphorbiaceae	Root Bark Fruit Leafmidrib

Station: Palayamkottai

Date :

Authorized Signature

Dr. S. SUTHA, M.Sc.,M.Ed.,Ph.D.,
Associate Professor
Dept. of Medicinal Botany
Govt. Siddha Medical College
Palayamkottai. Tirunelveli - 2.

ANNEXURE-V.I

DISEASE CRITERIA

GOVT. SIDDHA MEDICAL COLLEGE & HOSPITAL

PALAYAMKOTTAI - 2

DEPARTMENT OF POTHUMARUTHUVAM

A Prospective open labelled Phase II Non - Randomized Clinical Study of NELLI KUDINEER for RATHAMOOLAM (Bleeding Hemorrhoids)

Name : ……

Age/ Gender :……

DISEASE CRITERIA FOR ASSESSMENT*Raakhi Mehra,et al,Ayu.2011)*

Sl.No	Parameter	Grade 0 (G0)	Grade 1 (G1)	Grade2 (G2)	Grade3 (G3)
1	Bleeding Per Anus	Nil	Mild (Occasionally)	Moderate (Weekly/Monthly)	Severe (On each defaecation)
2	Pain around anus	Nil	Mild (Lasts for < 1 Hr	Moderate (Last for 1-2hr)	Severe (Last for>2hrs)
3	Constipation (Bristol stool scale)	Nil	Mild (Type 2) (on alternate days)	Moderate (Type 2) (2-3 days)	Severe (Type I) (>3 days)
4	Protrusion of pile mass	Nil	Protrude into analcanal,no prolapse.	Prolapse out of anal canal,spontaneous reduction	Prolapse out of anal canal,manual reduction.
5	Mucous discharge.	Nil	Mild	Moderate	Severe
6	Itchy anus	Nil	Mild	Moderate	Severe
7	Anemia [Hb (g/dl)]	Nil	Mild Men : 11-12.9 Women :11-11.9	Moderate (8-10.9)	Severe (<8)

ANNEXURE-V. 2

CASE SHEET REPORT OF OP & IP

CASE SHEET OF 20 PATIENTS TREATED IN OP FOR RATHAMOOLAM

Sl no	OP no	Name	Age/ gender	Occupation	Duration of illness	Date of onset treatment	Date of termination of treatment	Total days
1	31681	Sreenivasan	40/M	Cook	6 months	05.04.18	04.05.18	30
2	34770	Sabeena	32/F	House wife	1 year	16.04.18	15.05.18	30
3	38621	Epzi	42/F	Office work	2 months	30.04.18	30.05.18	30
4	42498	Prema	60/F	House wife	5 months	14.05.18	13.06.18	30
5	45205	Swarnapadma	45/F	House wife	2 years	24.05.18	23.06.18	30
6	47092	Kalaivani	46/F	House wife	2 years	31.05.18	30.06.18	30
7	50077	Inbarakavan	20/M	Student	1 year	12.06.18	11.07.18	30
8	50288	Kannan	39/M	Driver	1 year	13.06.18	12.07.18	30
9	52145	Risvana	23/F	Student	1 month	20.06.18	19.07.18	30
10	53878	Habeeba	20/F	Student	1 year	26.06.18	25.07.18	30
11	57212	Murukan	28/M	Carpenter	1 year	09.07.18	08.08.18	30
12	60525	Mumthaz	43/F	Tailor	3 months	20.07.18	19.08.18	30
13	61648	Sudalaimuthu	47/M	Cook	6 months	24.07.18	23.08.18	30
14	63912	Sundar	45/M	Marketing	2 months	01.08.18	31.08.18	30
15	67485	Sanmugam	49/M	Salesman	2 months	14.08.18	13.09.18	31
16	81122	Manikandan	25/M	Police	1 year	01.10.18	31.10.18	30
17	85158	Jayalakshmi	60/F	Teacher	1 year	16.10.18	14.11.18	30
18	97696	Suresh	40/M	Supervisor	1 month	26.11.18	25.12.18	30
19	10193	Stalin	60/M	Supervisor	3 year	03.12.18	01.01.19	30
20	533	Noorjahan	22/F	IT	6 months	02.01.19	31.01.19	30

CASE SHEET OF 20 PATIENTS TREATED IN IP FOR RATHAMOOLAM

Sl no	IP no	Name	Age/ Gender	Occupation	Duration of Illness	Date of admission	Date of termination	Total no of days
1	1360	Krishnaveni	30/F	Tailor	2 years	22.05.18	21.06.18	30
2	1783	Kuruvammal	37/F	Housewife	1 month	13.07.18	12.08.18	30
3	1918	Anthoniyammal	31/F	Housewife	6 months	27.07.18	26.08.18	30
4	2141	Madathi	60/F	House wife	7 months	22.08.18	21.09.18	30
5	2216	Esumani	60/F	House wife	2 months	29.08.18	28.09.18	30
6	2394	Nallammal	53/F	Tailor	1 year	22.10.18	21.11.18	30
7	2715	Mariyammal	50/F	Cook	3 year	08.11.18	07.12.18	30
8	2804	Ravi	22/F	Field work	1 month	16.11.18	15.12.18	30
9	2938	Lalithasenbakam	60/F	House wife	1 year	01.12.18	01.01.19	30
10	2987	Manonmani	59/F	Cook	8 months	07.12.18	06.01.19	30
11	3016	Arumukam	60/F	Cook	1 year	10.12.18	09.01.19	30
12	3047	Pechiyammal	55/F	Cook	8 months	11.12.18	10.01.19	30
13	96	Sivaraman	43/M	Driver	1 year	20.01.19	19.02.19	30
14	267	Muthu	53/F	Cook	1 1/2years	06.02.19	07.03.19	30
15	296	Subbulakshmi	58/F	Cook	2 years	08.02.19	11.03.19	30
16	312	Makavathi	39/F	Tailor	1 year	09.02.19	11.03.19	30
17	416	Mallika	50/F	Tailor	8 months	25.02.19	26.03.19	30
18	505	Selvi	52/F	Cook	3 years	27.02.19	28.03.19	30
19	606	Pandarathi	60/F	House wife	1 year	08.03.19	07.04.19	30
20	650	Chellammal	60/F	House wife	2 years	13.03.19	12.04.19	30

BLOOD INVESTIGATION CHART FOR OUT-PATIENT

SI No.	OP NO.	BEFORE TREATMENT						AFTER TREATMENT					
		Hb	TC	DC			ESR	Hb	TC	DC			ESR
				P	L	E				P	L	E	
1	**31681**	**11.8**	7000	60	38	02	8	**11.8**	8100	62	28	10	8
2	**34770**	**10.1**	7300	65	32	03	4	**10.2**	7000	60	36	04	4
3	**38621**	**11.5**	7400	52	45	03	14	**11.8**	7500	68	28	04	14
4	**42498**	**10.9**	8000	70	26	04	4	**11**	8100	70	28	02	4
5	**45205**	**10.5**	7200	62	36	02	4	**10.6**	7600	60	36	04	4
6	**47092**	**11**	8300	62	32	06	16	**11**	8000	62	33	05	16
7	**50077**	**13.5**	7500	62	35	03	26	**13.5**	5500	63	34	03	14
8	**50288**	**12.5**	8700	64	32	04	26	**12.5**	8400	64	33	03	12
9	**52145**	**10.4**	8200	62	34	04	24	**10.4**	7000	62	34	04	20
10	**53878**	**11.1**	7000	60	36	04	12	**11.1**	6400	66	26	08	8
11	**57212**	**12.1**	7300	64	29	07	32	**12.1**	7500	62	36	02	28
12	**60525**	**11**	8500	65	29	06	18	**11.1**	8000	64	30	06	18
13	**61648**	**12.5**	8400	64	32	04	24	**12.5**	6400	65	32	03	24
14	**63912**	**12.6**	6400	56	40	04	14	**12.6**	6800	58	40	02	14
15	**67485**	**8.3**	7000	65	31	04	64	**9.6**	7800	66	30	04	60
16	**81122**	**11.9**	8800	59	37	04	32	**11.9**	9000	60	38	02	30
17	**85158**	**9.1**	7500	68	30	02	14	**11**	8400	68	30	02	12
18	**97696**	**13**	8000	52	45	03	16	**13**	7500	68	28	04	18
19	**10193**	**12**	6200	60	36	04	20	**12**	6100	64	30	06	20
20	**533**	**10.6**	4200	64	34	02	4	**10.8**	4500	64	31	03	4

BLOOD INVESTIGATION CHART FOR IN-PATIENT

SI No.	IP NO.	BEFORE TREATMENT						AFTER TREATMENT					
		Hb	TC	DC			ESR	Hb	TC	DC			ESR
				P	L	E				P	L	E	
1	**1360**	**9.2**	8000	66	28	06	25	**9.3**	6500	60	34	06	20
2	**1783**	**8.4**	7800	65	31	04	20	**8.6**	7500	66	30	04	30
3	**1918**	**11.5**	9800	70	26	04	18	**11.7**	8900	68	28	04	15
4	**2141**	**12.5**	9000	58	38	04	15	**12.5**	7200	65	33	02	10
5	**2216**	**11**	8000	62	36	02	8	**11.3**	8000	62	36	02	8
6	**2394**	**9.4**	7100	58	37	05	50	**9.5**	7000	60	34	06	35
7	**2715**	**11**	8200	60	35	05	35	**11**	8000	62	36	02	20
8	**2804**	**13**	7100	62	32	06	10	**13**	8000	58	38	04	10
9	**2938**	**11.6**	8600	60	24	16	20	**11.7**	8100	60	36	04	15
10	**2987**	**11.9**	8800	64	30	06	5	**10**	7800	64	32	04	5
11	**3016**	**11.5**	6800	58	38	04	30	**11.5**	7000	60	38	02	30
12	**3047**	**12.1**	7000	65	32	03	10	**12.1**	6400	60	36	04	12
13	**96**	**14**	8000	64	30	06	40	**14**	8500	66	31	03	40
14	**267**	**12.1**	9100	54	44	02	20	**12.1**	9500	60	33	07	15
15	**296**	**10.3**	8100	64	32	04	45	**11.5**	8000	66	28	06	40
16	**312**	**13**	8100	60	38	02	70	**13**	8400	62	28	10	50
17	**416**	**10.4**	8100	60	35	05	10	**10.5**	8100	60	38	02	10
18	**505**	**11**	6500	61	35	04	20	**11**	6500	60	36	04	25
19	**606**	**10.8**	7500	62	36	02	5	**11**	7500	64	32	04	10
20	**650**	**6.2**	9600	66	31	03	30	**7.8**	7000	62	38	00	20

URINE INVESTIGATION CHART OF OUT-PATIENT

SL NO	OP NO	BEFORE TREATMENT			AFTER TREATMENT		
		Albumin	Sugar	Deposits	Albumin	Sugar	Deposits
1	31681	Nil	Nil	Nil	Nil	Nil	Nil
2	34770	Nil	Nil	Nil	Nil	Nil	Nil
3	38621	Nil	Nil	Nil	Nil	Nil	Nil
4	42498	Nil	+	Few ept cells	Nil	Nil	Nil
5	45205	Nil	Nil	Nil	Nil	Nil	Nil
6	47092	Nil	Nil	Nil	Nil	Nil	Nil
7	50077	Nil	Nil	Nil	Nil	Nil	Nil
8	50288	Nil	Nil	Nil	Nil	Nil	Nil
9	52145	Nil	Nil	Nil	Nil	Nil	Nil
10	53878	Nil	Nil	Nil	Nil	Nil	Nil
11	57212	Nil	Nil	$Bact_{+}$	Nil	Nil	Nil
12	60525	Nil	Nil	Nil	Nil	Nil	Nil
13	61648	Nil	Nil	Nil	Nil	Nil	Nil
14	63912	Nil	Nil	Nil	Nil	Nil	Nil
15	67485	Nil	Nil	Nil	Nil	Nil	Nil
16	81122	Nil	Nil	Nil	Nil	Nil	Nil
17	85158	Nil	Nil	Nil	Nil	Nil	Nil
18	97696	Nil	Nil	Nil	Nil	Nil	Nil
19	10193	Nil	Nil	Nil	Nil	Nil	Nil
20	533	Nil	Nil	Nil	Nil	Nil	Nil

URINE INVESTIGATION CHART OF IN-PATIENT

SL NO	IP NO	BEFORE TREATMENT			AFTER TREATMENT		
		Albumin	Sugar	Albumin	Sugar	Albumin	Sugar
1	1360	NIL	Nil	Nil	Nil	Nil	Nil
2	1783	+	Nil	Nil	Nil	Nil	Nil
3	1918	Nil	Nil	Nil	Nil	Nil	Nil
4	2141	Nil	Nil	ET cell+	Nil	Nil	Nil
5	2216	Nil	+	Nil	Nil	Nil	Nil
6	2394	Nil	Nil	Nil	Nil	Nil	Nil
7	2715	Nil	Nil	Nil	Nil	Nil	Nil
8	2804	Nil	Nil	Nil	Nil	Nil	Nil
9	2938	Nil	Nil	Nil	Nil	Nil	Nil
10	2987	Nil	+	Nil	Nil	Nil	Nil
11	3016	Nil	Nil	Nil	Nil	Nil	Nil
12	3047	Nil	Nil	Pus cells+	Nil	Nil	Nil
13	96	Nil	Nil	Nil	Nil	Nil	Nil
14	267	Nil	Nil	Nil	Nil	Nil	Nil
15	296	+	Nil	Nil	Nil	Nil	Nil
16	312	Nil	Nil	Nil	Nil	Nil	Nil
17	416	Nil	Nil	Nil	Nil	Nil	Nil
18	505	Nil	Nil	Nil	Nil	Nil	Nil
19	606	Nil	+	Nil	Nil	Nil	Nil
20	650	Nil	Nil	Nil	Nil	Nil	Nil

ANNEXURE-VI

PROCTOSCOPIC EXAMINATION

Proctoscopic view: IP no- 650 (BT)

Proctoscopic view: IP no- 650 (AT)

ANNEXURE-VII

RESEARCH METHODOLOGY & BIOSTATISTICS CERTIFICATE

The Tamil Nadu Dr. M.G.R. Medical University

69, Anna Salai, Guindy, Chennai - 600 032.

This certificate is awarded to Dr/~~Mr/Mrs~~.....M. Sumayya.....

*for participating as **Resource ~~Person~~** / Delegate in the XXIII Workshop on*

"RESEARCH METHODOLOGY & BIOSTATISTICS"

Organized by the Department of Siddha,

The Tamil Nadu Dr. M.G.R. Medical University from 6th to 10th March 2017.

Dr. N. KABILAN, M.D.(Siddha)
PROF & HEAD
Dept of Siddha

Dr. T.BALASUBRAMANIAN M.S.,D.L.O.,
REGISTRAR

Prof. Dr. S.GEETHALAKSHMI, M.S.,Ph.D.,
VICE CHANCELLOR

ANNEXURE-VIII

CME CERTIFICATE-1&2

GOVERNMENT SIDDHA MEDICAL COLLEGE& HOSPITAL
PALAYAMKOTTAI

CME PROGRAMME

Conducted by
SIRAPPU MARUTHUVAM
DEPARTMENT
GSMCH - PALAYAMKOTTAI

Organised by
VAIDYARATNAM

Supported by

S.No: 135

CERTIFICATE

This Certifies that
Dr. M. Sumayya.
has participated in Continuing Medical Education on "AYUSH External Therapies-II" held at GSMCH, Palayamkottai on Dec, 4 2018

Dr. A.S.Poongodi Kanthimathi MD (S).,
Head - Dept. of Sirappu Maruthuvam

Authorised Signatory
VAIDYARATNAM

Dr. R. Neelavathy MD (S), Ph.D.,
Principal

GOVERNMENT SIDDHA MEDICAL COLLEGE
PALAYAMKOTTAI, TIRUNELVELI – 627 002
CONTINUING MEDICAL EDUCATION PROGRAMME

Conducted by
Post Graduate Department of Pothu Maruthuvam

This certificate is awarded to Dr / ~~Mr~~ / Mrs.....SUMAYYA.M.....
has participated in the CME Programme held on 05.12.2018 at Conference Hall, Special Therapy Wing, Government Siddha Medical College, Palayamkottai, Tirunelveli. This programme is focused on "HIV / AIDS"

Prof .Dr.A.MANOHARAN , M.D (s) , (Ph.D)
Head , Department of PothuMaruthuvam
Government Siddha Medical College,
Palayamkottai

Prof . Dr. R. NEELAVATHI, M.D(s)., Ph.D.,
Principal
Government Siddha Medical College
Palayamkottai

ANNEXURE-IX

1.CERTIFICATE OF PUBLICATION-1

Certificate of Publication

PRINT ISSN No : 2249-555X | Index Copernicus (IC) Value : 86.18 | Impact Factor : 5.397

This is to certify that

Mr./Mrs./Ms./Prof./Dr. Sumayya.M

has contributed a paper as author/ Co-author to

INDIAN JOURNAL OF APPLIED RESEARCH

A Peer Reviewed, Refereed, Refereed & Indexed International Journal

Title "ACUTE AND CHRONIC TOXICITY STUDY OF SIDDHA HERBAL FORMULATION NELLI KUDINEER SAMULAM"

and has got published in volume 09, *Issue* 04, APRIL-2019

The Editor in Chief & The Editorial Board appreciate the Intellectual Contribution of the author/co-author

Executive Editor | *Editor in Chief* | *Member, Editorial Board*

ANNEXURE-IX

2.FRONT PAGE OF JOURNAL PUBLICATION-1

Original Research Paper

Volume-9 | Issue-4 | April-2019 | PRINT ISSN No 2249-555X

Ayurveda

ACUTE AND CHRONIC TOXICITY STUDY OF SIDDHA HERBAL FORMULATION NELLI KUDINEER SAMULAM

Sumayya. M* — PG Scholar, Department of Maruthuvam, GSMC, Palayamkottai, Tamilnadu, India *Corresponding Author

Manoharan. A — Professor, Head of the Department, Department of PothuMaruthuvam, GSMC, Palayamkottai,Tamilnadu, India

ABSTRACT **BACKGROUND:** The Plant (Herb) is still considered among the important source of bioactive compound, especially in Siddha medicine that has been used for long periods. The Nelli Kudineer (NK) has been mentioned in classical Siddha literature *GunapadamMooligai Vaguppu(Murugesa Mudaliyar C.S.2013)(1)* for the management of *Rathamoolam (Shanmugavelu K.N.,2003)(2)* and it has been correlated symptoms in modern medicine is Bleeding Haemorrhoids.

OBJECTIVE: The objective of this study was to investigate the acute and Chronic toxicity of Siddha herbal formulation Nelli Kudineer (Samulam).

METHOD: Acute toxicity and chronic toxicity of Nelli Kudineer (NK) is carried out as per the OECD-423 guidelines. In the acute toxicity study were used in female albino Wister rats, single and multiple enteral dose (60,300,2000 mg/kg) for 14 days administered all group of treated animals. At the end of the study, the trial animals are sacrificed and results were recorded.

RESULTS: The results are assessed for the effect of Nelli Kudineer. Animals body weight, relative organ changes, haematological, biochemical and histopathological parameters showed good progress. In the acute and chronic toxicity studies no mortality or behavioural changes were observed in treated rats used in Nelli Kudineer (2000 mg/kg) indicating that the LD 50 was less than Value is P 0.05.

CONCLUSION: These results exhibit the absence of acute and chronic toxicity after treatment of Nelli Kudineer was observed. So, all the results were revealed NK is safer and high therapeutic uses in long period.

KEYWORDS : Nelli Kudineer, Amla, Siddha Medicine, Toxicity studies.

INTRODUCTION

In clinical practice, Nelli Kudineer was used in ano-rectal disorders, especially in rathamoolam(Haemorrhoids). Moolanoi is a common problem in a modern word, because diet and life style is more prevalence and incidence of disease. NK is basically astringent in nature and reduces the dilated blood veins. The "*Rathamoolam*" is in *IngiVaiyaChinthamani-800.(Ramachandran S.P.,2013)(3)* it can be correlated in Modern Medicine as Bleeding Haemorrhoids. All the veins are lined with valves that permit blood to flow in only one direction (back to the heart). Excess pressure on these valves can cause them to weaken and fail, allowing blood to flow in the wrong direction or to stagnate, it causes haemorrhoids.

The Nelli Kudineer, was majorly composed of Phyllanthus Emblica (Linn.) Phyllanthaceae family. The tree is small to medium in size, reaching 1–8 m (3 ft 3 in–26 ft 3 in) in height. The branchlets are not glabrous or finely pubescent, 10–20 cm (3.9–7.9 in) long. The fruit is nearly spherical, light greenish yellow, quite smooth and hard on appearance, with six vertical stripes or furrows (Yoganarasimhan 2000). It is Sour, Astringent and Sweet in taste, Cold potency, sweet in division as per Siddha Literature (Murugesan 2013). Amla is an extremely rich source of vitamin C. It also balances the both Pitham and Vaatham by virtue of sweet taste. The Kapham is balanced primarily due to its drying action. So it is essential to evaluate the safety and toxicity of the Nelli Kudineer, before their uses in human health. Preclinical toxicity studies are necessitate for determining a safety profile.

MATERIALS AND METHODS

MATERIALS

Collection and Authentication

The parts of Nelli were freshly collected from Tenkasi, Tamilnadu areas and identified by the Gunapadam department experts at Government Siddha Medical College and Hospital, Palayamkottai. Whole part of amla used in this study.

PURIFICATION AND PREPARATION

The adulterants from the raw drugs were removed, cleaned and dried in shade. The purified raw drugs were coarsely powdered and taken as a Kudineer Chooranam form.

EXPERIMENTAL ANIMALS

The female Wister albino rats, weighing 180-200g±20 were taken in this study. All animals were maintained under standard laboratory conditions of temperature (22±2 °C) and humidity 50±15% with 12 h day 12 h night cycle. Rats had free access to water and rodent pellet diet (Hindustan Lever Ltd, Bangalore, India). Animals were acclimatized to laboratory conditions one week prior initiation to the experiments.

TOXICITY STUDY METHOD:

Acute and chronic toxicity of Nelli Kudineer is carried out as per the guidelines (OECD) 423. After the animal ethical clearance from Institutional Animal Ethics Committee (KMCP/29/1.5.18).

ACUTE ORAL TOXICITY

The female Wister albino rat are fasted over night and provided only water, after which the Nelli Kudineer is administered by gastric intubation to Group1 animals orally administered the dose of 50 mg.kg^{-1} body weight in *Nelli Kudineer*. The animals are then observed for 14 days and maintained with normal food. No mortality rate were observed after 14 days, all the animals are noted, no toxic effects were observed in this study., then the same dose is repeated again for confirmation. However. The procedure is repeated for further higher doses such as 300 and 2,000 mg.kg^{-1} body weight. No mortality of animal is noted. Toxic symptoms are observed for 72 hrs including behavioral changes, locomotion, convulsions and mortality (Shetty Akhila et al 2007 & Shah Ayub et al.1997, Bürger et al.2005)(4,5,6)

Cage Side/Histopathology Observations:

All the animals were observed, including the changes in skin, eyes, mucous membranes, respiratory, circulatory, autonomic and central nervous systems, and somatomotor activities are noted. End of experiment no tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma were noted. Body weight, food and water intake are recorded at two-day intervals. Surviving animals are fasted overnight, weighed and humanely killed on the 15th day using anesthetic ether. All test animals are subjected to gross necropsy.

Chronic toxicity for Nelli Kudineer

The Male and female Wister albino rats weighing 180-200 ± 20 g are used for the present study. The animals are divided into five groups of six animals in each group. The animals in Group I are administered 0.5 ml Tween orally for 90 days. In Group II are administered with 50 mg.kg^{-1} b.w. of the Nelli Kudineer orally once daily for 90 days. The animals in Group III are administered with 100 mg.kg^{-1} b.w. of the Nelli Kudineer orally once daily for 90 days. The animals in Group IV and V are administered once daily with 200 and 400 mg.kg^{-1} b.w. of the Nelli Kudineer for 90 days orally (Pierre,*et al* 2006, Joshi, *et al* 2007,

ANNEXURE-IX

3.CERTIFICATE OF PUBLICATION-2

European Journal of Pharmaceutical and Medical Research

SJIF Impact Factor: 4.897 (EJPMR) ICV 79.57

Date: 03/06/2019

CERTIFICATE FROM EDITOR

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ANNEXURE-IX

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QUALITATIVE PHYTOCHEMICAL ANALYSIS AND ANTI-MICROBIAL ACTIVITY OF SIDDHA HERBAL PREPARATION NELLI KUDINEER (AMLA)

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ABSTRACT

Phytochemical is a compound responsible for color and biological properties of plants. The term is generally used to refer to those chemicals that may have biological significance but are not established as essential nutrients. The Qualitative Phytochemical analysis and anti microbial activities of Nelli Kudineer (*Phyllanthus emblica*(L.)) have been determined from this study. The Harborne et al.(1998) methodology was used for phytochemical analysis. The alcoholic extract of Nelli Kudineer (NK) have some chemical active substances that produce a definite physiological action and therapeutic uses in the human body. The Qualitative Chemical screening of alcohol extract of NK is revealed the presence of various secondary metabolites such as Alkaloids, Phenols, Glycosides, Steroids, Tannins and Terpenoids. The Nelli Kudineer has Zonal inhibitory concentration of anti-microbial activity against *E.coli* and *Staphylococcus aureus* which is assayed by Agar-Well Diffusion method.

KEYWORDS: Nelli Kudineer(Amla), Qualitative Phytochemical analysis, ZIC, Anti-microbial activity.

INTRODUCTION

Phyllanthus Emblica(L.), *Emblica officinalis* Gaertn, *Mirobalanus emblica* Burm. family Euphorbiaceae. Amla is moderate sized deciduous tree with grey or red bark which is peeling off in scales and long stripes. Leaves are alternate and distichous, the branchlets resemble pinnate leaves and stipulate are narrow or absent. The flowers are small, monoecious and are axillary. Capsules are 3-crustaceous or coriaceous 2-valved cocci, berries or drupes with 3-4 celled stone. The seeds are trigonous. The bark yields leucodelphinidin, procyanidian, 3-O-gallated prodelphinidin and tannin. The seed contains vitamin C, Carotene, Nicotinic acid, Riboflavin, D-glucose, D-fructose, Myoinositol and Pectin with D-galacturonicacid, D-arbinosyl. The pharmacologicl activities of NK has an Alterative, Tonic, Adrenergic, Anti-cholinergic, Anabolic, Anti-bacterial, Anti-bilious, Anti-cancer, Anti-convulsant, Antidote, Anti-inflammatory, Anti-oxidant, Anti-pyretic, Laxative, Hepatoprotective activities. Various parts of amala is useful for Anaemia, Anorexia, Ascites, Asthma, Bleeding, Cancer, Constipation, Diabetes, Haemorrhoids, Inflammation (James et al. 2006). The alcoholic extract of fruit has been proved anti-bacterial, anti-viral activities and rich source of Ascorbic acid and important phytochemical is Pectin, Ellagic acid and Gallic acid.

Literature review

Pandey Govind and Pandey(2011) have done the work of phytochemical and acute toxicity study of Emblica officinalis, at the end of study he found 250,500 and 1000mg/BW of F.albino rats, which showed LD50 for more than 1000mg/kg and further he determined hydro alcoholic extract of Emblica fruit showed the presence of alkaloids, glycosides, tannins and steroids. Shubhi mehrotra et al(2010) had determined the anti biotic activity of Emblica is effective against three target pathogens, viz S.aureus, V.cholerae and P.aeruginosa, ZIC is 0.025,0.025 and 0.025(ug/ul) respectively. Antony B et al.(2008) done a Pilot clinical study to evaluate the effect of dried extract of amla 500 and 1000mg/day was administered two times a day for six months, at the end of study he determined the reduced lipid level and lowering CRP levels. Further he established the extract was contained 35% galloellagi and tannins. Gunkitidechakul N et al.(2010) have observed that the aqueous extract of amla containing tannins(43%), uronic acid(11%) and gallic acid(21%) was effective in delaying and reducing DMBA-induced and (12-otetradecanoylphorbol-13-acetate)-promoted skin carcinogenesis in mice. Qari Muhammed Kaleem et al.(2014) studied on Emblica derived Tannins for their Immunostimulatory and Protective activities against Coccidiosis in Industrial Broiler Chickens. The Study revealed that Tannins has vital role in humoral immune response in Sheep red blood cells (SRBCs) by haemagglutination assay($P \leq 0.005$).

ANNEXURE-X

PLAGIARISM CERTIFICATE

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Urkund Analysis Result

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